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THE

AMERICAN JOURNAL

OF THE MEDICAL SCIENCES

OCTOBER, 1925

ORIGINAL ARTICLES.

THE RELATIONSHIP OF THE SYMPATHETIC INNERVATION TO THE TONE OF SKELETAL MUSCLE.

By the late John I. Hunter, M.D., Ch.M.

SYDNEY, AUSTRALIA.

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[This essay was written for this Journal by the late Professor Hunter on board the vessel that brought him from America to England in November, 1924. His aim was to reply to the criticisms of his work that had been made during the previous two months in America and also to clear away certain misunderstandings. It was merely the first draft, but it is published here exactly as he left it without any alterations of any sort.—G. Elliott Smith.]

"It appears to me likely that reflex tonus is the expression of a neural discharge concerned with the maintenance of *attitude*." Sherrington, "The Integrative Action of the Nervous System," 1920, p. 340.

I. **Introductory.** It has been known since 1879 that striated muscle receives not only motor nerve endings from the thickly medullated cerebrospinal nerves, but also the terminations of non-medullated nerve fibers which form a rich plexus lying between the muscle fibers. Tchiriev, the discoverer of this fact, regarded these terminations, which are grape-like in appearance, simply as immature forms of the typical motor nerve endings. Consequently from the physiological standpoint his investigations did not excite a great deal of interest. But the fact observed by him that the "terminations en grappes" were connected with non-medullated nerve fibres

and the typical motor endings with medullated nerve fibres suggested that some specific difference existed between the two modes of innervation. Obviously, however, histological examination alone was not adequate to decide this point. For instance in 1913 Boeke suggested that the non-medullated fibres were sympathetic or autonomic in character. But it has been the application to this problem of the histo-experimental method by Boeke, Boeke and Dusser de Barenne and Agduhr which has proved beyond reasonable doubt within the last decade that the vertebral sympathetic ganglia are the source of these fibres. In other words the non-medullated nerve plexus is made up of post-ganglionic fibers of the sympathetic nervous system, the term "sympathetic" being employed here in the sense defined by Langley. It refers to the system of nerve cells and nerve fibres which have a connexion with the cerebrospinal axis limited to the thoraco-lumbar region. Fig. 1* represents schematically the principle of the operations employed by Boeke in investigating the source of the double innervation of the extrinsic muscles of the eye. In one series of experiments one of the motor cerebral nerves to the extrinsic muscles of the eye was removed near its point of emergence from the brain stem. Conversely, in the other series, the superior cervical ganglion was removed. While open to question in certain important details, Boeke's general interpretation of his results, namely, that some, at least, of the non-medullated nerve fibres supplying the eye-muscles are transferred to the oculo-motor nerves, by way of the cervical sympathetic trunk reaching the nerves distal to the point of emergence of these nerves from the brain stem, is unquestionably justified. Further a similar operation and its converse have been performed more recently upon spinal nerves. Boeke and Dusser de Barenne and Agduhr have both produced degeneration of all the medullated nerve fibres to certain muscles by section (of both anterior and posterior nerve roots) of the appropriate spinal nerves, while non-medullated fibres supplying these muscles remained intact. Conversely Agduhr found the remains of degenerated non-medullated fibres in preparations of the interosseous muscles of the cat's fore paw six days after removal of the ganglion stellatum.

It has been established therefore that striated muscle has a double innervation, *i. e.*, from the somatic cerebrospinal medullated nerves and from the sympathetic nervous system. The latter nerve supply consists of non-medullated fibres of cells in the vertebral sympathetic ganglion which reach the spinal nerve by way of the grey rami communicantes. Impulses from the cerebrospinal axis proceed to the sympathetic ganglion by way of the white rami communicantes which arise in the thoraco-lumbar region.

* Although no figures accompanied the manuscript, the text is left unaltered so that the article may be entirely Dr. Hunter's. There are indications that a bibliography was intended, but it has not been supplied for the same reason.—Ed.

The non-medullated fibres and their endings are independent of the sympathetic terminations upon the bloodvessels supplying skeletal muscle. Sometimes, it is true, they accompany arterioles to the muscle, but as they approach their site of termination they proceed to the muscle fibres entirely independently of the vascular plexus, as Dr. Oliver Latham and I have shown in a memoir now being prepared for publication.[1]

II. **The Function of the Sympathetic Innervation of Striated Muscle.** In 1913 de Boer, as the result of experiments upon frogs, claimed to have shown that the sympathetic nerve supply of skeletal muscle was concerned with tone. He believed that the tone of striated muscle was governed exclusively by its sympathetic nerve supply. All subsequent workers have shown that this contention is untenable. De Boer's view is being replaced by the conception that only a certain element of muscle tone is due to the sympathetic nervous system. In 1915 Langelaan advanced the view that the tone of skeletal muscles consists of two elements, one component being governed by the somatic supply and the other by the sympathetic innervation of the muscle. This suggestion was put forward independently by Revon. Later, Langelaan (*Brain*, 1922), as the result of experiments on frogs adduced further evidence in confirmation of his opinion. He failed, however, to clear away the fundamental objection to the acceptance of his theory, namely, that no investigator had shown tone to be altered consistently in decerebrate preparations as a result of sympathetic denervation; or, conversely that decerebrate rigidity could develop if the sympathetic innervation were left intact but the somatic nerves severed.

The importance of the decerebrate preparation consists in the fact that from its study in the hands of Sherrington and others, most of the prevailing ideas of muscle tone are derived. Sherrington proved that the tone of skeletal muscle was postural in function. He found that the typical position of the decerebrate animal was that of "reflex standing," with all four limbs rigidly extended, and the neck retracted to a greater or lesser degree. Between these phases there were periods in which the limbs were no longer maintained in extension. During these periods, or when the extension of the limbs was overcome by passive movement, the musculature was found to exhibit a condition of "plasticity." If the leg were flexed at the knee, so lengthening the extensor muscle of the thigh this position was retained ("lengthening reaction"). If the knee were now extended, so shortening the extensor muscle the new position was again maintained ("shortening reaction"). Sherrington (*Brain*, 1915) called the property of skeletal muscle, which enabled it to exhibit these reactions, "plastic tone." He emphasized the fact that the degree to which this property was exhibited was independent

[1] Since published in *The Medical Journal of Australia*, January 10, 1925.

of the length of the muscle fibres exhibiting it. And very correctly, following the suggestion of Grützner and others, he compared this property of skeletal muscle to that of involuntary muscle, such as that of the bladder wall, which enables it to adjust itself to enclose an increasing volume under practically the same wall-tension. Speaking of this comparison Sherrington says: "Both are instances of the postural contraction of muscle; though the relation of the central nervous system to the postural activity is very different in the two cases." For Sherrington believed that the tone of striated muscle was entirely dependent on the intactness of the somatic motor nerve supply, while involuntary muscle can exhibit tone in the absence of its innervation.

The objection to the view that the tone of skeletal muscle is partially governed by the sympathetic nervous system on the ground of the inconsistent and negative results of experimentors employing the decerebrate preparation for investigating this problem disappears now that Royle's and my experiments and surgical operations have demonstrated the influence of the sympathetic. In this work evidence of the connexion of the sympathetic innervation with the tone of skeletal muscle is forthcoming not only from experiments upon the decerebrate goat but from the effect of sympathetic ramisection in patients suffering from forms of spastic paralysis, which, prior to operation revealed all the essential qualities of decerebrate rigidity. In normal, spinal, and decerebrate animals, and in human patients, sympathetic denervation of the limb musculature led to *a consistent qualitative alteration in muscle tone.* The defect was found to be a lessening of the efficiency of the muscle in maintaining a position once it had been assumed. This was the case whether the position had been imposed passively, reflexly, or by voluntary contraction, and as I have previously argued (*Brain*, 1924) is due to the same fundamental change namely, the loss of plastic tone. In the decerebrate preparation, after passive movement, the limb deprived of its sympathetic innervation failed to maintain the new position imposed upon it either when the extensor muscles were lengthened or shortened. Instead, the limb would fall back to a posture determined by the action of gravity and the length of the fibrous tissues composing it. This illustrates the effect of sympathetic denervation to remove plastic tone, as evidence of which is the absence of the "lengthening and shortening reactions" of Sherrington. The skeletal muscles of human patients show a similar qualitative alteration. This is clearly shown for instance, in one of Dr. Royle's patients with spastic paraplegia supervening upon a gunshot wound of the cortex. Prior to operation this patient clearly exhibited "lengthening and shortening reactions" of the extensor muscle of the knee. Before operation if the left thigh were lifted from the bed the unsupported leg would remain extended for a long period of time. If the extended leg were

passively flexed at the knee-joint it would remain flexed in its new position. If it were now passively extended the extended position would be maintained. After left lumbar sympathetic ramisection these reactions, which are identical with the "lengthening and shortening reactions" of the decerebrate preparation described by Sherrington were no longer exhibited, *i. e.*, plastic tone was removed by the operation.

But it is important to notice that tone does not entirely disappear after sympathetic denervation. Only one efferent pathway to the skeletal muscle has been removed. The remaining somatic innervation is responsible for another component of muscle tone. In the acute decerebrate preparation, for instance, notwithstanding the removal of its sympathetic nerve supply, the typical extensor attitude of the limb is assumed. The neuro-muscular mechanism concerned in imposing the extended position is obviously intact; *i. e.*, the medullated somatic nerves are responsible for this function. It will readily be seen that the extensor muscles must be shortened in order that the extensor attitude of the limb may be attained. The antagonistic muscle groups, on the other hand, are reflexly inhibited, as Sherrington's studies of the acute decerebrate preparation have shown. Their component of tone, which is somatic in origin, and is exhibited as a degree of contraction of selected muscle groups may, following Langelaan, be called "contractile tone."

Contractile and plastic tone are both postural in function. Contractile tone imposes posture as a result of shortening of appropriate muscle groups; plastic tone takes part in maintaining this posture once it has been attained by fixing the length of the muscle exhibiting contractile tone. On account of the responsibility of these two components of tone in the production and maintenance of posture they may together be referred to as constituting postural tone.

As Sherrington's deafferented preparations show, the production of postural tone depends upon the existence of proprioceptive impulses. Posterior nerve root section in all the spinal segments connected with a given muscle removes both contractile and plastic tone. Impulses arising in the muscles, therefore, discharge through both the somatic motor nerve roots and the white rami of the sympathetic nervous system. In other words contractile tone is subserved by a somatic proprioceptive reflex arc; plastic tone is governed by a sympathetic and reflex arc. On account of the limited connexions of the sympathetic nervous system with the spinal cord, these reflex arcs for a given muscle group are usually situated at different levels of the central nervous axis. Purely spinal reflexes are, however, inadequate in higher vertebrates for the exhibition of the postural tone responsible for the natural attitudes of the body. The reflexes responsible for the extensor attitude of the lower extremities depend, for instance, upon reflex arcs which pass as

high as the pons in the brain stem. It appears that the vestibulo-spinal tract is the descending limb of the reflex arc subserving the contractile tone to the extensor muscles of the limb; while plastic tone depends upon a reflex arc the descending limb of which is constituted by the ponto-spinal tracts. I have recently argued that these reflex arcs are governed by the tectum, substantia nigra, and red nucleus of the midbrain, the corpus striatum, and the cerebral cortex by way of the cerebellum. The influence of all these structures upon postural tone is produced ultimately through both the somatic and sympathetic efferent connexions to skeletal muscles. In other words there are two final common pathways to such muscles. The excitatory impulses emerging through the somatic motor pathway to provide muscle tone give rise to contraction of the muscle and contractile tone. The effect of the excitatory impulses emerging through the sympathetic rami communicantes is to fix the existing length of the muscle (plastic tone). It is obvious that this is a primary subdivision of postural tone according to the properties subserved by the two efferent connexions of skeletal muscle. The sources of the impulses emerging through each pathway are numerous in each case, as already mentioned. Both connexions are in fact final common pathways in the sense of the term employed by Sherrington.

III. **Technique of Experiments in which the Decerebrate Animal was Employed to Determine the Effect of Removing the Sympathetic Innervation of Skeletal Muscle.** The negative and inconsistent results obtained by previous investigators employing the decerebrate preparation to determine the function of the sympathetic innervation of skeletal muscle call for comment. The following points appear to have been of importance in leading to the success of the experiments of this kind in the hands of Dr. Royle.

1. *The Interval between Two Stages in the Operation.* In our earlier experiments the lumbar portion of the sympathetic trunk was removed from one hind limb in goats. This was done as a preliminary procedure. Then, at a variable period after this operation, decerebration was performed. In the first series the interval between the two operations varied from seven to seventy-three days. The best contrast between the hind limbs on the operated (left) and inoperated (right) side was seen in the animal in which the interval between the operations had been longest. In this animal extension of the left limb was easily overcome in contrast to the opposite limb. When not handled with the animal lying in the fixed supine position, the left limb rapidly fell from its temporary position of extension to a passive posture of semi-flexion. In this stage of relaxation the "lengthening and shortening reactions" were absent.

Kulchitsky has demonstrated (*Journal of Anatomy*, January, 1924, p. 160) that "the medullated and non-medullated fibres never

terminate in the same muscle fibre." In other words each voluntary muscle is formed partly of actively contractile fibres innervated by somatic nerves and partly of striated muscle fibres, which are not contractile (although their length may be altered passively by the contractile fibres). The latter are innervated by post-ganglionic sympathetic fibres and their activity is controlled by the sympathetic ganglia under the influence of the white rami communicantes of the thoracico-lumbar outflow from the spinal cord.

These three observations depend upon the loss of plastic tone. The comparative ease in performing passive flexions of the extended limb is due to the fact that contractile tone, which is responsible for thus imposing this position, alone has to be overcome, to alter the position. On the intact side while contractile tone is responsible for the position of extension it is assisted by plastic tone, which tends to fix the length of the muscles necessary to maintain this position. When contractile tone is overcome on the partially denervated side, no further resistance to movement is offered. On the opposite side though resistance suddenly gives way when reflex shortening of the extensor muscles (*i. e.*, contractile tone) is overcome, some degree of resistance to passive flexion is still maintained, which is to be attributed to the existence of plastic tone. As Walshe has pointed out this phenomenon has its counterpart in the clasp-knife effect of decerebrate rigidity.

Some decerebrate rigidity is due to the presence of an exaggerated degree of both contractile and plastic tone. The extended position imposed by contractile tone due to the selective reflex shortening of the extensor muscles is rigidly maintained by the fixation of the extensor muscles in their shortened state by plastic tone. In the absence of plastic tone this rigid fixation is no longer apparent and the limb fails to maintain the extended posture once the reflex shortening of the extensors (dependent upon impulses emerging through the intact medullated somatic nerves) ceases. The active posture of extension is now no longer maintained.

When the limb was passively extended or relaxed spontaneously it would fall into a semi-flexed position determined by gravity and the length of the fibrous tissues contained within the limb. If the knee joint were now passively flexed or extended the leg would resume its original posture. In other words a passive posture characterized the limb instead of the ability to occupy active postures, which is the property of the normal musculature in the decerebrate preparation. For the "shortening" and "lengthening reactions" are no longer exhibited, *i. e.*, plastic tone is absent.

Unquestionably these three manifestations of the loss of plastic tone are not so clearly exhibited when the interval between lumbar sympathectomy and decerebration is short, *e. g.*, when decerebration is performed in the same day as that on which the lumbar

sympathetic trunk is removed. I have records of three decerebrate preparations which exhibited the "lengthening and shortening reactions" in this way when both procedures were carried out on the same day. In each of these however the resistance to passive flexion and the tendency for the maintenance of the extended position were definitely less than on the control side.

The explanation of the progressive loss of plastic tone may be that this property of skeletal muscle is less dependent upon impulses emerging from the central nervous system than is contractile tone. In this respect skeletal muscle would resemble, to a certain degree, smooth muscle, the tone of which is not absolutely dependent upon its nerve supply. There are difficulties in supporting this analogy, because recovery in the tone of involuntary muscle following denervation of involuntary muscle occurs as time advances. But in view of the fact that only some muscle fibres receive sympathetic nerve fibres and are therefore alone responsible for the property of plastic tone, it is feasible that these denervated "fixing" fibres slowly lose this property after sympathetic denervation, so differing from the neighbouring "movement" fibres, which are absolutely dependent for their property of contractile tone upon the intactness of the central connexions of the somatic nerve fibres that supply them. Moreover in the lumbar operation, so far employed, it is necessary to bear in mind that all the sympathetic ganglia from which the gray rami to the lower limb arise are not removed though efferent impulses to them from the spinal cord are not removed. This fact may, in some measure, perhaps account for the progressive loss of plastic tone. The entire question, however, of the determination of the time necessary to produce the complete effect after sympathetic denervation is under examination. It can best be settled by studying the effects of the operation in the chronic decerebrate animal described by Bazett and Penfield. The introduction of the interval operation disposes of certain statements which have been made previously to explain the changes seen following sympathetic denervation. In the first instance diminution in tone cannot be ascribed to sensory inhibition due to the wound inflicted in performing the operation of sympathectomy. For, ample time is provided to allow healing of the wound to occur. Nor are the changes due to vasodilatation because the diminution in tone permits, or even increases in degree, although the vasomotor changes are a maximum immediately after the operation (*cf.* Bayliss, Hartman, Blatz and Kilborn). Sympathetic ramisection in human patients affords similar results in this direction: for the loss of plasticity has persisted for twelve months in the case of the first patient subjected to operation, although obvious vasomotor changes were only present in the first few weeks (Royle). In other patients the circulatory disturbance has been of greater duration but it had a general ten-

dency to be reduced in degree though the loss of plastic tone was still apparent. Some of the effects upon tone of sympathetic ramisection may, however, be due to the attendant increase of blood supply to the limb. I refer to its effect upon contractile tone. Dr. Royle has noticed, for instance, that cold has less effect in increasing contractile tone in the limb of a spastic paraplegic which has been subjected to operation than in the limb of the opposite side. As the result of vasoconstriction the limbs of the spastic paralytic are invariably colder than normal. The advent of vasodilatation with an attendant increase in temperature of the limb lessens the degree of contractile tone. This reduction is greater immediately after the operation than it is subsequently: for the vasomotor changes become less marked as time proceeds. But the reduction in plastic tone progresses in the opposite direction.

2. *The Method of Examination of the Animal.* After removal of the sympathetic innervation of one limb the otherwise intact goat can walk, and run, in the normal manner. The characteristic change produced by the operation is revealed, however, if the animal is placed in the supine position with its head held rigidly in the midline. All limbs take up an extended posture under these conditions, but as Dr. Royle has shown, when all cause for alarm is removed by gentle handling of the animal, the lower limb of the operated side falls from the extended position into a passive posture determined by mechanical factors. This method of examination for changes in the postural tone of the limb was adopted with advantage for the decerebrate preparation. The goat is placed in the supine position in a cradle and the head is held firmly in the median line or the animal is first encased in a leather jacket which fits round the trunk and neck and then placed in the cradle. In this way the effects of the tonic labyrinthine and neck reflexes of Magnus and de Kleijn are excluded. Under these conditions the typical extensor posture, as already explained, is assumed by all four limbs. But after a short period the limb which has been deprived of its sympathetic innervation falls under the action of gravity to a passive posture of abduction and semi-flexion.

By this method of examination any defect in the maintenance of posture is readily indicated by failure of the skeletal musculature to support the weight of the limb. This is a matter of importance: for efforts to test for diminution of tone by passive movement set up a reflex spasm of the musculature of the limb, which is evidence of the excitability of the nervous connexions responsible for contractile tonus. Clinicians are familiar with this observation, for spastic muscles may before palpation show no evidence of an increased degree of contraction, but a reflex tonic contraction is set up immediately passive movement is attempted. In the first phase the posture is maintained predominantly by plastic tone. After

examination of the limb is commenced increased contractile tone is superadded. Obviously the effect of passive movement will be to obscure any diminution in the degree of plastic tone.

Nevertheless passive movement overcomes contractile tone alone more easily than contractile and plastic tone combined, as has already been discussed.

3. *Avoidance of the Effects of Asphyxia and of Anemia of the Brain Stem.* It is clear from the foregoing argument that the results of loss of plastic tone would be more difficult to observe if any condition existed which would unduly increase the degree of contractile tone. As Dr. Royle (*The Medical Journal of Australia*, September 27, 1924, p. 315) has pointed out, asphyxia of the animal would produce this effect. To avoid this complication he employed intratracheal anesthesia and then oxygenated the animal freely as soon as decerebration was performed. If asphyxia tended to develop later, *e. g.*, when the tube in the trachea was too small, the rigidity in extension of all four limbs would become extremely marked and differences in the tone of the hind limbs (due to the loss of plastic tone on one side) would be markedly obscured. Removal of the cause of asphyxia would invariably remove the tendency for the display of such an exaggerated degree of contractile tone. In recent papers Walshe has argued from physiological evidence, that minimal degrees of oxygen in like manner may lead to hyperexcitability of reflex arcs. Evidence is accumulating that this factor may account for so-called "irritative" symptoms following central nervous lesions. But the effects of asphyxia and anemia, which are manifested as reflex hyperexcitability, are foreign to the condition of tone decerebrate rigidity. Like the state of spastic paralysis this condition is to be regarded as being due to a release of function in the nervous system, following the removal of higher levels of nervous activity. The term release is employed in the sense advocated by Hughlings Jackson, and developed in the present century by the work of Head and his collaborators. For this reason it appears to me that the Sherrington method of decerebration, which should be carried in the goat by section of the midbrain under direct vision, is preferable, for the purpose of observing the presence or absence of plasticity, to the method of decerebration by anemia induced by combined ligation of the carotids and basilar arteries which has been introduced by Pollak and Davis. While such a preparation is unquestionably most useful for observing the reflex activities of such an animal, it is impossible to be certain in how great an area of the brain stem the cell stations are hyperexcitable due to the presence of a degree of anemia which is insufficient to abolish function altogether.

4. *The Choice of Laboratory Animal.* The animal selected for the operations, in the first instance, was the rabbit. Dr. Royle

procured an excellent result, consisting in the diminution in tone of the hind limb of a spinal rabbit on the side from which the lumbar sympathetic trunk had been removed. This effect was not reproduced in subsequent experiments and this failure was attributed to the difficulty in this animal of completely excising the sympathetic trunk on the selected side without injury or removal of the trunk of the opposite side. Therefore the goat, which had already been studied by us in connexion with the problem of determining the factors responsible for the symptomatology of complete transverse lesions of the spinal medulla, was employed in subsequent mammalian experiments. In this animal the lumbar sympathetic trunk is large, well defined, and easily traceable from the upper lumbar region to the level of the common iliac artery. It is separated from its fellow of the opposite side by a wide interval. In this way Dr. Royle's experiments, upon the effect of removal the sympathetic trunk on decerebrate rigidity, came to be performed on an animal with simple postural reflex activities of the limb musculature. "Reflex standing" is beautifully illustrated in the well oxygenated decerebrate goat. This is especially true of the hind limbs in which the degree of rigidity is invariably as great, or may be greater than in the fore limbs. With the goat in the fixed supine position loss of plastic tone becomes apparent by early failure in the maintenance of the extended posture of the defective limb. This observation was identical with that already made on such an animal prior to decerebration. In contrast to the goat, a carnivorous animal such as the cat shows a capacity for great variation in the degree of postural tone. The cat does not take up the extensor posture, when placed in the supine position. Variation in the degree of contractile tone in its four limbs impose varied attitudes upon it, and no doubt in the well oxygenated decerebrate cat the variations in the degree of rigidity of the limbs which are encountered are to be accounted for in a like manner. Such variations in the degree and selective activity of contractile tone possibly make the effects of loss of plastic tone less apparent than would otherwise be the case and render an analysis of the exact defect in tone more difficult at the outset. For it must be borne in mind, in this connexion, that in the experiments recorded in the literature, all of which were performed on cats, differences in the degree of tone upon the two sides follow unilateral sympathectomy, which was performed in some cases before and in others after, decerebration. For instance Dusser de Barenne observed a diminution in tone in five cases out of nine, after midlateral removal of the lumbar sympathetic chain. Uyeno found differences in the tone of the fore limbs after removal of the ganglion stellatum on one side, but attributed the diminution in tone to sensory inhibition due to the wound on this side. In Royle's experiments this explanation is not admissible. Consequently the problem present-

ing itself is not to explain negative results but inconsistent results. I believe that the factors to which attention has been called in the foregoing discussion explain the failures encountered. This is especially the case when it is recognized that investigators in the past have been seeking to observe quantitative diminution of tone. I have attempted to show that contractile tone is well displayed after sympathetic denervation and under certain experimental conditions may be present in an enormously exaggerated degree. It is only when qualitative changes due to the selective removal of plastic tone are looked for that the interpretation of effects in any such instance becomes clear.

The thesis maintained in this paper that plastic tone is a property of the sympathetic innervation of skeletal muscle no longer rests upon the evidence provided by experimental decerebrate rigidity. For the same effect as that which follows sympathetic denervation in the decerebrate animal is produced by sympathetic ramisection in men in those conditions of spastic paralysis and the extended form of paraplegia, which exhibit all the essential qualities of decerebrate rigidity. The excessive plastic tone characterizing these conditions is removed by the operation. The evidence of this fact which may be obtained by studying the character of the knee jerk is of special interest. For in both decerebrate rigidity and in the types of spastic paralysis to which reference has been made, the slowness in execution of the knee jerks became brisk in character. This is due to the rapid rate of relaxation of the extensor muscle after completion of the jerk contraction which replaces the former tendency of the muscle to remain shortened ("shortening reaction") when contraction ceases.

Further the evidence adduced by Langelaan, as the result of his work on frogs, is in favor of the view that plastic tone of skeletal muscle is subserved by its sympathetic innervation. I have been able to confirm Langelaan's observations by a series of experiments on the influence of the double innervation upon the posture of the wing of birds. These experiments include the unmasking of plastic tone by removing the somatic innervation, subsequently rendering the plastic wing flaccid by removal of the influence upon it of the cervical sympathetic trunk. But this paper has been confined to a discussion of the effect of sympathetic denervation upon the muscle tone of the decerebrate preparation. The reason for this is that most of the scepticism in regard to the validity of any theory which relates the sympathetic innervation to the tone of skeletal muscle, has been aroused in the past by the failure of various workers to modify consistently the onset or development of decerebrate rigidity by sympathectomy.

SOME NOTES ON CANCER.

II.

On Human Intestinal Parasites as a Cancer Inciting Factor and on the Significance of the Precancerous State.*

By Willy Meyer, M.D.,
NEW YORK.

On basis of extensive studies of the literature on cancer the writer, in a previous paper (I),[1] emphasized the utter improbability of the existence of a specific causative cancer microörganism. He endorsed the opinion of those who consider it no longer tenable to have an open mind with regard to that question. With them he took the stand that where cancer appears to be due to the action of bacilli, it arises, as in other cases, from chronic irritation, in this case from the irritation emanating from the bacilli. Continued study of the literature has only deepened that conviction.

It may not be inappropriate, once more briefly to point out the difference in the attitude to cancer genesis of the adherents of the specific theory and of those of the nonspecific theory, making use for this purpose of certain work of Yamagiwa.[2] That author said (1905) at the end of a set of theses: "There is no specific microorganism of cancer." A few years later, when Fibiger, by means of a nonspecific worm, had produced the first experimental primary carcinoma, Yamagiwa felt stimulated by that great success into attempting to prove his thesis by other nonspecific means and, together with Ichikawa, produced the first experimental primary tar carcinoma (1913).

In these experiments, on removal every third or fourth day of the previous tar application before putting on the new coat, not infrequently bits of epidermis would be torn off with the hardened tar crust, causing slight hemorrhages. The nonspecifists consider such lesions as rather inconsequential. But the specifists—and there are those whose opinion commands attention—see in them the gate for the entrance of the alleged ubiquitous specific cancer parasite into the system of the animal that is being tarred. They deny the contention of the nonspecifists that long-continued irritation of tissue by means of a nonspecific substance is of itself, and exclusively, responsible for the observed experimental result, that is, the primary carcinoma at the point of application of the irritant, and claim that not the irritant, but the presence of the

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about-to-be-discovered specific agent is the cause of the observed cancerous process.

"Admissible in medicine," says Orth,[3] "is any hypothesis and theory competent to give a satisfying explanation of verified observations; but no hypothesis and no theory that lays claim to consideration can afford to disregard established facts." It appears proper then to inquire, how by means of the specific theory the case of Niebergall,[4] for instance, can be explained, in which myomata, polypi, sarcoma and carcinoma were found in the same uterus, or the case of Petersen,[4] who found a tumor having grown expansively (*i. e.*, benign fashion) into the depth and progressively (*i. e.*, malignant fashion) in a lateral direction.

The concomitant of the cancer bacillus is, of course, the cancer serum. From Adamkiewicz's cancroin, thirty years ago, down to our day serum after serum has been brought out, every one of them prepared from an isolated alleged specific cancer microörganism. Just now there seems to be a recrudescence of such efforts. However, even a successful cancer serum would prove nothing for the specific theory. It would merely be another instance of the well-known fact that injected foreign protein may make more or less impression on diseased tissue. But in order to do that the protein does not have to be of bacterial origin, nor must the diseased tissue necessarily be cancerous. The possibility that injection of foreign protein into a cancer patient should occasionally create the illusion, temporarily at least, of a complete recession of the tumor, is freely conceded; but the result cannot be repeated at will; it just accidentally happens. Moreover, such retrogression has dangers; the serum is apt to destroy the cancer cells so quickly and thus flood the system with the decomposition products of cancer cells in such quantity, that the system cannot cope with this poison, and the patient dies from getting better. Proper dosage might perhaps be found if all cancers were alike; but they are all different, and consequently, at best, a serum treatment in cancer, by its very nature, must, as regards dosage, always remain guess work. So from whatever point of view we look at the effort to find a specific cancer microörganism, it appears to be an endeavor leading in all probability nowhere, even if successful.

For these and other previously expressed reasons[1] the writer has joined the ranks of those cancer students who have definitely written "finis" under the "specific" chapter of cancer etiology. But not satisfied with assuming a purely negative stand, the writer is trying to obtain insight into the genesis of cancer by plodding in the cancer literature, carrying together therefrom mutually supporting experimental results, observations and deductions, analyzing them and arranging them in logical sequence, with the idea in mind of focussing the consensus of opinion and of getting at the trend of it.

In my first communication on cancer,[1] nonspecific parasites came

in for more or less attention. Inasmuch as all the numerous, though otherwise unrelated cancer-inciting factors lead up to the same result, namely cancer, it appeared of no particular consequence which one of them should be selected for more detailed study. It was, therefore, thought best to continue with the parasites.

The human intestinal parasites, helminths,[5] so far as medicine is interested in them from the point of view of cancer, are various nematodes, trematodes and cestodes. The life histories of these parasites have certain features in common:

1. They all have no less than three stages of development, ovum, larva, worm; and (excepting only Trichinella spiralis, the larvæ of which are born alive, without the preceding deposition of an ovum) they come in contact with man in all three stages. Those of the parasites in question which have more than three stages of development, go through the additional stages in intermediate hosts, molluscs and fishes, but come in contact with man also only in the same three stages, as do those which have but three.

2. All the parasites in question, at certain periods of their evolution, require a complete change of nutritional environment for the attainment of the next stage of their development, that is, they require a change of hosts or they require a temporary life in the open air or in water and subsequent return into a host.

3. In the larval stage all the parasites in question migrate more or less extensively within the human body, quite a number of them following a certain typical route: from the intestine to the lungs, to the pharynx and back to the intestine, and only by the performance of this circuit can those asexual larvæ develop into sexual worms.

4. All these parasites, as stated in my first communication,[1] are organotrope, that is to say, they exhibit an apparent predilection for one organ or another, and in that organ they make their habitat. The reason for this phenomenon is undoubtedly the fact that they find there the medium best suited to their nutritional requirements and the conditions which, in respect of their anatomical peculiarities, facilitate the satisfaction of these requirements. What enables a special parasite to link up with a special organ remains unexplained, unless the assumption be accepted as an explanation that the parasites swarm all over, but that only those survive which reach the suitable environment.

On reflection, the feature around which best to group the proposed discussion appeared to be this fact that all these parasites come in contact with man as ova, as larvæ and as worms, as all three stages, in one or the other of the parasites, have been found to enter into the causation of precancerous conditions.

Ova as a Cancer-inciting Factor.—Ripe ova of ascaris (Küchenmeister, *et al.*[6]) and the embryos of tapeworms (Braun, p. 250[5]) have

been demonstrated (Shinohara[7]) on garden fruit and green vegetables. Against eating such raw food Metchnikoff[8] warned from the point of view of danger of infection with parasites. Borrel,[9] in 1908, repeated that warning from the point of view of cancer, and again in 1923, a warning in which the International Cancer Congress held at Strassbourg concurred by general resolution.

Under normal conditions the smooth ova of roundworms (nematodes) and tapeworms (cestodes), as ordinarily deposited in the lumen of the intestine, are harmless; but it will be seen below that in cases where ascaris worms (nematodes) or adult liver flukes (trematodes) force an entrance into the liver or gall bladder or pancreas, the ova there deposited by them contribute their share toward the injurious consequences of such invasion.

Harmful of themselves, on the other hand, are the spiked ova of the Bilharzia parasites (trematodes).[10] These worms live in the portal venous system, and their ova are normally deposited in the capillaries of the pelvic venous plexuses, vesical, rectal and genital. Only a small part of the total number of ova so deposited reach the evacuating channels; billions are left behind in the tissue, die there and are calcified (Lortet and Vialeton, pp. 12, 60, 96[10]) so that the infested tissue becomes completely saturated with innumerable minute pointed particles of lime or chalk, an ever-present source of severe irritation. On section such tissue creaks under the knife (Chaker, p. 33[10]).

Infestation with Bilharzia takes place in the larval stage of the parasites, the larvæ entering through the skin or mucous membranes when these organs come in touch, through drinking, bathing or walking barefoot on wet ground, with water contaminated with the larvæ. Among town dwellers, with little or no chance of reinfection, the majority of cases rarely get beyond the first symptom of bilharziosis: hematuria (Milton[10]), which is so common in Egypt as to be almost universal and to be scarcely considered abnormal.[11] But among the rural population (fellahs), whose work with bare arms and bare limbs in the irrigated fields and irrigation ditches of the lower Nile Valley exposes them to frequent reinfection, the ravages of the disease for which no real remedy is known, are appalling. In these severe cases the disease takes the form of papillomatous degeneration of the mucous membrane of the bladder, or of the bowels including the rectum, and of polypous growths arising from the submucosa (Küchenmeister, *et al.*),[12] which necrose, separate at their pedicles and result in ulcerations of dysenteric appearance.[13] So also does bilharziosis of the glans penis give rise to ulcerations.[14] All these ulcerations are caused by the chronic irritation of the tissue arising from the calcified ova. They are chronic, nonhealing lesions; as such they are a precancerous state. In course of time a certain percentage of such lesions become definitely cancerous.

Very large accumulations of Bilharzia ova have also been found in

the seminal vesicles and in the glands and organs contributory thereto (Chaker, pp. 36, 37[10]) and have been demonstrated in the ejaculated sperma (Lortet and Vialeton p. 14[10]), an occurrence to which the term ovispermia has been applied.[15] It is a fair presumption that ova from that source may find lodgment in the mucous membrane of the vagina, adhering thereto with their spikes. A male bilharziosis patient who was positively not reinfected and was kept under constant medical supervision as many as ten consecutive years, at the end of that period still discharged daily, undiminished quantities of ova (Lortet and Vialeton, pp. 14, 16, 17[10]). Not unlikely, therefore, in a long married life, the husband having bilharziosis, Bilharzia ova may accumulate in the vagina of the previously healthy wife in quantity sufficient to induce therein primary lesions of the severity of those seen in the bladder and in the rectum of the fellahs. This may occur in a woman whose cervix uteri, bladder and rectum are perfectly healthy—proof that the ova did not come from within, but came from without. There is a case on record where such a history of the growths found in the vagina was strongly suspected (Madden).[16] But the occurrence is probably not as infrequent as the fact of there being—as far as I was able to find—only one such case reported, and that incomplete, would seem to suggest. Young Egyptian boys are proud when seized with hematuria, considering it a sign of attained manhood. Without reinfection the hematuria which they can see subsides in the course of years, but the nonvisible ovispermia remains as a danger for their prospective wives. The women of the agricultural population of Egypt never see a doctor, and the men do so only when they "drop in their tracks." As it is just in this class of people that conditions such as stated would be most likely to occur more often, scarcity of observation cannot be considered as reflecting on the likelihood of the occurrence (Milton, Madden, Lortet and Vialeton,[10]).

There would then have been found here a strong probability of a real "cancer à deux," not that fabled one of the alleged transfer in married couples of cancer cells or of an imaginary specific cancer microörganism from one partner to the other; but the actual transfer per coitum of a nonspecific cancer-inciting factor, namely, spiked calcified ova, from the Bilharzia infested husband to the previously uninfested wife, with the prospect of a primary vaginal cancer in the wife.

There are, of course, numbers of women in Egypt and elsewhere who contract bilharziosis the same as do the men, by primary infestation, especially the fellah women who are assisting in the work in the fields. In them bilharziosis of the vagina is said to be very frequent and to take the form of an acute vaginitis (Fantham, p. 643[5]).

Common in such cases is also the involvement of all parts of the

vulva in the bilharzic process, principally of the labia minora, where warty masses are seen, shaped like bunches of currants and comparable to condylomata acuminata (Koch, p. 55[5]). There occur in them also polypoid tumors in the cervix uteri. One such, the size of a hen's egg, reported from Mauritius, on being excised, creaked under the knife and, on microscopical examination, was found to consist of dense strands of fibrous tissue enclosing Bilharzia ova. "The diagnosis of the origin of these growths, so common here in Mauritius," says the author, "leads one to expect that many similar cases are to be found in other tropical countries where bilharzia disease is common."[17]

American interest in bilharziosis is not so far removed as it would seem to be on first impression. Considering the heavy tourist travel to Egypt and contiguous countries, the possibility of visitors acquiring bilharziosis is a matter of rather considerable actuality. Most all open water courses, lakes, ponds and pools near human habitations in Africa and in the contiguous southerly parts of Asia Minor contain Bilharzia larvæ. The same as in the case of hookworm larvæ (p. 67[18]), the mere touching of the skin with gloves or socks wetted with Bilharzia-contaminated water is probably sufficient for infestation to take place. During the World War many of the soldiers from Australia and India, quartered in Egypt, fell victims to bilharziosis for which, as stated, there is no known remedy,* and the question of how to handle them after they returned home, to prevent the importation of the disease into previously clean districts, became quite a problem. The two danger points are: (1) The discharge of ova with the feces or urine of Bilharzia patients into or near fresh water; (2) the presence in the water of suitable molluscs. Where the latter are wanting there is no danger of the spread of the disease (Manson, p. 63[10]).

Summary of Section on Ova. 1. Precancerous lesions, nonhealing superficial ulcerations, are produced by the spiked ova of the Bilharzia parasites in the bladder, the bowels, the rectum and the genitals.

2. Bilharzia ova have been demonstrated in the ejaculated human sperma ("ovispermia").

3. Ova having a smooth surface can become a contributory factor in the production of precancerous lesions, as for example, when liver flukes and ascaris worms deposit ova in the gall bladder and in the bile ducts of the liver, or in the ducts of the pancreas.

Larvæ as a Cancer-inciting Factor.—Mention was made above of the typical migration in the human system of the larvæ of some of these parasites over a well-defined circuit, from the intestines by various routes to the lungs, thence to the pharynx and back to the intestines.

* Recent reports announce promising results of tartarus stibiatus, given intravenously.

In this connection an interesting phenomenon has been observed in the migration of hookworm larvæ through lymph glands, especially the inguinal and axillary glands. The larvæ arrive there performing the characteristic larval wiggling motion by which they force their way through the cell masses. After a while the pace of some of them is retarded, owing to lymph cells attaching themselves firmly to their surface. For a while the larvæ drag the load along, but eventually, though still wiggling, make no more headway; soon the wiggling also ceases and the result is an asphyxiated larva, lying dead in the gland, buried in a thick envelope of lymph cells.[18] The same fate has been observed to overtake ascaris larvæ in the pleural sac.[19] Such captured larvæ then undergo necrobiosis with consequences similar to those discussed further down with reference to worm nodules.

As regards the lesions in tissues and organs owing to their penetration by migrating larvæ, light has been sought thereon by experiment.

1. "On flooding a young pig with ascaris larvæ, both lungs were found greatly swollen, edematous, intensely hemorrhagic, the color of liver, and extensively hepatized. Microscopically the pathological picture varied from that of an acute lobular pneumonia in which the areas of inflammation centered around the bronchioles, to lobar pneumonia in the stage of red hepatization. A photomicrograph showed areas of consolidation, the alveoli being almost entirely filled with serosanguinolent exudate, also extensive immigration of leukocytes and the round-cell infiltration characteristic of acute inflammation, and, in other portions, enlarged alveoli, indicating a compensatory emphysema" (p. 22[20]).

2. On flooding the system of a young guinea pig with hookworm larvæ, one lung became "solidified with blood and the other contained numerous larger and smaller hemorrhagic spots" (Dock and Bass[21]). Mechanical injury could not have caused the latter, because ecchymoses have been observed in such cases in the axillary and inguinal glands prior to the arrival of the larvæ therein; the ecchymoses rather appear to be due to the concentration in the system of toxins from the mere massive invasion of hookworm larvæ (Looss, p. 53[18]).

3. In a similar experiment the liver was found diffusely affected, not only with such hemorrhages, but also with necrotic spots; in the immediate neighborhood of the latter were observed hypertrophic liver cells and numerous mitotic cell divisions, while at some distance from the same were located a great many round, well-defined tissue infiltrations, consisting mostly of leukocytes and, in many instances, containing larvæ.[21]

As regards the bearing of the foregoing observations on human conditions, flooding of the human system with ascaris larvæ is not a likely occurrence, because for every ascaris larva migrating therein,

a ripe ascaris ovum must first have been ingested, and that does not usually happen in quantities.

The same applies to the embryo of the tapeworm (Braun, p. 250[5]), of which ordinarily one or a few are ingested at a time. Occasionally however, the position of the tapeworm in the intestine may become reversed and in vomiting,[21] especially during pregnancy (Küchenmeister, p. 13[5]), ova-carrying links of the worm are then apt to get lodged in the stomach. In that event hundreds and thousands of ova will be set free in the stomach at the same time, flooding the system with tapeworm embryos which then develop therein into cysticerci, that is, larvæ (Frangenheim, p. 464[21]).

Mass infestation of the human system is also a possibility in the instance of hookworm larvæ and Bilharzia larvæ, both of which invade the host through the skin. In the extreme case of such mass invasion, the lesions due to the migration of the larvæ may have cancerous potentialities, as indicated by the third experiment.

As a rule, however, in the human being, the lesions resulting from this on first impression so formidable looking phenomenon, that is, the migration of the larvæ, will hardly ever be sufficiently severe, or sufficiently lasting, to assume precancerous characters.

Encapsulated Larvæ. In contradistinction to the migrating larva the resting encapsulated larva appears to be frequently the inciting factor of cancerous developments. Light has been thrown on this matter by experiments on frogs which were infected with nematodes.[22] The migration of larvæ was here experimentally produced in the frogs, and the day-to-day progress of the induced phenomena of migration and encapsulation was established by a series of 85,000 sections. The processes set up in these capsules in frogs are not generally recognized as actually malignant.[23] Did the critics perhaps overlook the fact that metastases were formed (Kopsch, p. 115[22])?

Even more monumental is a long line of experiments on the conditions surrounding the encapsulated Cysticercus fasciolaris in rats (Bullock and Curtis).[24] In these researches the number of primary sarcomata experimentally produced exceeded 1000 in September, 1924.

These two so widely differing investigations seem to agree in a number of observations and deductions, which are: (1) That of several adjoining capsules only one may become cancerous; (2) that the point of origin of the active process is in the connective-tissue envelope of the capsule; (3) that at the beginning of the process only a small part of the envelope is involved; (4) that the onset of invasive growth appears to be conditioned on the presence of the live larva.

The reasons advanced for this latter assumption (point 4) are in the instance of the larval nodules in frogs the observation that nodules containing dead larvæ, as also nodules abandoned by the

larvæ after they had formed around them, did not become malignant, and that only those nodules showed invasive proliferation which contained a live larva (Kopsch, pp. 58, 114, 117[22]).

In the case of the cysticercus cysts in rats[24] the condition of the larvæ in cysts which had assumed malignant properties seemed to depend upon the state of preservation of the cyst wall. "When the cyst wall was partly uninvolved by the tumor, or consisted largely of healthy tumor tissue, the parasite was alive and intact, but when the transformed cyst wall was involved in the tumor-necrosis, the larva was usually dead and distorted and even necrotic and fragmented."

From this observation the investigators made the deduction "that the live larva probably initiates the malignant process and that the death of the worm is secondary to the growth and necrosis of the tumor" (Bullock and Curtis, 1920, p. 169; 1924, p. 477[24]).

The onset of malignancy in a capsule Bullock and Curtis ascribe to "some influence as yet undetermined" (1920, p. 156[24]); Kopsch (p. 117[22]) suggests "secretions and excretions of the larva," Fibiger,[25] in the case of the experimental spiroptera carcinoma of the rat, "a toxin emanating from the worm."

With reference to the deduction that without the influences emanating from a live parasite the onset of invasive proliferation cannot take place, it may not be amiss to call again attention to facts mentioned in part in my first communication,[1] namely, the finding of lifeless objects at the center of cancerous growths, objects which with equal justification as the live parasites, it would seem, can be considered bound up with the initiation of those growths. The cases referred to are: A completely calcified cysticercus surrounded by an infiltrating glioma the size of an apple;[26] a sequestrum of the radius in a fibrochondrosarcoma thirteen years after a compound fracture of the forearm;[27] in two instances, needles at the center of malignant growths;[28] in another instance a thorn;[29] the occurrence of melanosarcoma in the sole of the foot of African negroes through trauma from walking through thorny brambles;[30] the experimental production in rats of primary carcinoma of the tongue by means of bristles,[31] and finally a piece of glass free in the peritoneal cavity of a mouse, which, failing to pass the pylorus, had caused there the onset of true cancer and eventually had cut its way through.[32] Quite likely the chronic irritation produced by these inanimate substances was the inciting factor of the precancerous state from which developed the malignancy found surrounding them. If toxins were at work in the initiation of these invasive growths, as perhaps they were, the toxins in these cases certainly did not emanate from the inanimate inciting factor. Inasmuch as apparently the result of the effect arising from foreign inanimate as well as from foreign animate matter was the same, namely, malignant growth, it must be assumed

that both types of matter stand in a similar relation toward that growth, and that consequently parasites like inanimate factors, are not the direct cause of cancer, but the indirect cause of it, preparing the soil for it as it were; in other words, that these live parasites are also merely a cancer inciting factor, the initiators not of cancer, but of a precancerous state.

Summary of Section on Larvæ. 1. As a rule the lesions due to the migration of larvæ in the system appear neither sufficiently severe nor sufficiently lasting to cause the onset of a precancerous state.

2. In cases of frequently repeated massive larval invasion through the skin (hookworm, Bilharzia), or in cases of massive autoinfection (tapeworm), the migration of the larvæ may cause lesions having cancerous potentialities.

3. In contradistinction to the fact that migrating larvæ only exceptionally start the train of events ending in cancer, the resting, encapsulated larvæ are commonly found capable of becoming the inciting factor of precancerous conditions.

4. Whenever in such cases the precancerous state proceeded to definite malignancy the point of departure of the malignant process was found located in a small part of the connective-tissue envelope of the capsule of a live larva.

5. Inasmuch as dead matter, as well as a live larva, appears capable of inciting cancer the toxins emanating from the parasite probably merely cause the onset of a precancerous state, in other words, encapsulated larvæ would seem to be not the direct cause of cancer, but to be only of the dignity of a cancer-inciting factor. (See "General Summary" at end of article.)

Worms as a Cancer-inciting Factor.—Adult worms, ascaris and liver flukes, like larvæ, are frequently found to cause the formation of nodules in man; but the conditions surrounding the two cases are entirely different. While larval capsules and nodules as a rule enclose only 1, or at most 2 or 3 larvæ in the same capsule, worm nodules contain a great mass of worms as well as their ova and these ova, being smooth and consequently not capable of passive motion through the tissue, as are the spiked Bilharzia ova, stay where deposited (Koch, p. 59[5]).

An instructive instance of this kind is found in cases of long standing invasion of the liver with Distomum hepaticum in cattle (Küchenmeister, p. 99, ff[33]). These liver flukes crowd into a bile duct as long as there is room for one more, blocking the lumen. The bile stagnates and decomposes and becomes sticky or hardens around the worms and the ova deposited by them. The pressure of this solid mass, its effect as a foreign body and the necrobiotic toxins emanating therefrom, affect the mucous membrane of the duct, change it to a tendon-like consistency and turn the duct into a rigid tube. Eventually inflammatory processes set in, and when,

as frequently happens, the worms have invaded a blind duct, the entrance to the same is apt to be closed behind them by the proliferating tissue, making the worms captives. Such foci in the liver are seen to develop in time into hard nodes, the size of a nut, which can be palpated from the surface. Cattle are ordinarily killed before the development of the precancerous state, presented in the nodes, can have run its course, but there is nothing to interfere with the completion of the process when worms invade the liver, the gall bladder or the pancreas of the human being and create conditions therein similar to those described for cattle. Such was the case with some of the eaters of raw fish mentioned in the first communication,[1] who therewith ingested the larvæ of Opistorchis felineus, a liver fluke. Upon reaching the human intestine these larvæ develop into worms and then invade the common bile duct and the ducts of the organs resorting thereto, the total number of worms in the various ducts in some cases running up into thousands. Surrounding the worms the lumen of the ducts was found filled with epithelial detritus, leukocytes and the ova deposited by the worms. These worm nodules in the liver of human beings have in several instances been the point of departure of primary gelatinous carcinoma (Rindfleisch,[34] Askanazy[35]). There were numerous metastases in the liver and in the epigastric lymph nodes (Rindfleisch 1910, p. 18[34]). The unusual parasite and the unusual type of tumor were advanced as the reason for connecting both as cause and effect. There were besides other indications that such was the case. The malignancy was here apparently due to the toxins proceeding from the necrobiosis of the worms and of that of the cellular detritus.

Ascaris worms, like liver flukes have a propensity for forcing their way into narrow channels. In the feces of an insane person who had the habit of swallowing small glass beads, adult ascaris worms were found wedged in the holes of the beads (Mosler and Peiper, p. 313[5]; Fantham, p. 687[5]). In two other cases ascaris worms were found with marks of strangulation on their bodies, their discharge under anthelmintic treatment having cured a jaundice of long standing (Koch, pp. 119, 120;[5] Fantham, pp. 688–689[5]). Direct proof of the invasion of the common bile duct and dependent organs by ascaris worms, was furnished by a series of observations made in the autopsy room in Manila (Crowell[36]). In the tropics ascaris worms are looked upon by medical men "with respect and fear." "Migration of the ascaris into the common bile duct and thence into the gall bladder or into the intrahepatic bile ducts is a frequent occurrence and must be much more frequent than is indicated by the reported cases, as the diagnosis is made only at operation or at autopsy." . . . "After the death of the worms in the bile duct they become macerated or flattened, stained with bile, and may become incrusted with bile pigments" . . . "Worms may pass into the duct of Wirsung and determine either

the formation of abscesses or the development of an acute hemorrhagic pancreatitis. It also seems probable that the ascaris in the common bile duct may so block it as to lead to the development of an acute hemorrhagic pancreatitis without the entrance of the worm into the duct of Wirsung" (Crowell,[36] Mosler and Peiper, p. 313[5]).

The common bile duct and the duct of Wirsung are both too narrow to admit of the passage of full-grown ascaris worms. In passing, note should perhaps be made of the fact that the full-grown ascaris worm is as large in an infant as it is in an old man seventy years of age.[37] Full-grown ascaris worms found in the liver, the gall bladder or the pancreas can, however, under no circumstances have developed therein from either ova or larvæ, as sometimes suggested by authors, but must have invaded the organs from the intestine as worms, because ascaris ova mature nowhere else but in the open air, and ascaris larvæ cannot become worms until they have migrated over the above-described circuit which ends in the small intestine. The invasion of the biliary system and of the pancreas by these parasites must therefore be taking place soon after the end of the larval migration, while the ascaris worms are still small. Even less possible is such development from ova or larvæ in the said three organs in the case of the liver flukes, the embryos of which hatch from the ova only in water, and the larvæ of which must have passed through two different intermediate hosts, a mollusc and a fish, before they can develop within the intestine of the definitive host into the worm.

In parenthesis, certain facts regarding liver flukes are here perhaps of interest, as connecting up with statements made above with reference to the spread of bilharziosis. Cancer from liver flukes as the inciting factor was first observed at the University of Königsberg. That town is located near a bay which averages 5 miles in width. The bay is cut off from the main body of the Baltic by a peninsula 60 miles long and 1 to 2 miles wide which consists entirely of high sand dunes. For ten years there had not been a single case of cancer among the 2300 inhabitants of the peninsula, while on the opposite low, swampy mainland there were many cases of cancer during that time, though type and habits of the people in both localities are identical.[38] On both sides of the bay the people are heavily infested with the tapeworm Bothriocephalus latus (Rindfleisch, 1910, p. 14[34]). The difference in the two localities consists in the fact of there being on the land side many fresh water streams which empty into the bay, and none such on the peninsula. As established for the nearby river Elbe,[39] so also these streams probably swarm with the immature larvæ of parasites requiring a mollusc for an intermediate host in order to attain the mature larval stage,[34] among them the larvæ of liver flukes which, after they have gone through the molluscs, which are plentiful in these streams, penetrate the scaly skin of the fish frequenting those waters and settle down

in the muscles of the same, developing no further until their particular host has been eaten by a warm-blooded being (cat, dog, man). On the peninsula, there being no streams, there are consequently no molluscs and, therefore, no larvæ of liver flukes in the fish. The inhabitants go fishing in their home waters. Those on the land side catch, and eat raw, fish infested with the larvæ of the liver flukes, those of the peninsula fish not so infested. Both catch and eat raw fish infested with the cysticercus of Bothriocephalus latus. Consequently tapeworm prevails on both sides of the bay, while only the inhabitants of the land side are infested with liver flukes. The latter being a cancer-inciting factor, cancer occurs on the land side, but none from that cause on the peninsula.[40]

Liver flukes, when full-grown, are only 1 cm. in length by 2 mm. in width. In the small intestine they do not seem to find the suitable environment and perish therein quickly (Rindfleisch, 1910, p. 21[34]); but thousands may be demonstrated in the liver and in the gall bladder. In such cases the latter has been found of the size of a walnut, its walls, as also those of the large ducts, being greatly thickened. Light pressure upon the gall bladder brought on the outflow from the papilla Vateri of a glassy mucus, in which masses of the worm were demonstrable (Rindfleisch, 1910, p. 4[34]). The worms are easily overlooked and not infrequently escape detection during operation. They are translucent and of a reddish hue, so that a convolute mass of them gives the impression of a "mucoid blood coagulum." Only by careful inspection, looking against the light, do they become discernible through reflection (Askanazy, 1904[35]). It is quite probable that invasion of the liver and of the pancreas by worms is much more frequently the cause of cancer in these organs, than is commonly supposed (Rindfleisch, 1910, p. 23[34]).

Summary of Section on Adult Worms. Dead adult liver flukes enclosed with their ova and with cellular detritus in nodules of the biliary system or in the pancreas, also adult ascaris worms that have invaded the ducts of these organs, may, probably by the combination of mechanical pressure, foreign body irritation and toxins, produce therein a precancerous state.

General Summary.* The three questions regarding the relation of ova, larvæ and worms to cancer incitement having been discussed, it should be mentioned again that they were selected for special consideration not so much because of the interest attaching to them *per se*, but rather as representatives of all the multifarious factors known to have set in motion, in one instance or another, a train of events which terminated in cancer. The task would, therefore, seem to remain of deducing from the foregoing and from the references features common to all the factors of which nonspecific parasites are a paradigm.

* See also the Summaries of the several sections.

1. Numerous, and among themselves unrelated factors, when impinging upon human tissue, are apt to irritate it and to set up therein a chronic morbid condition, from which a sequence of events culminating in cancer has been observed sometimes to arise. Such potentially cancerous conditions have, therefore, been termed a "precancerous state," [4i] and the factors inducing them, "cancer-inciting factors."

2. Cancer-inciting factors, while capable of initiating a precancerous state, evidently do not govern the behavior of the tissue during this state, for the suspicious condition of the tissue may be aggravated, or it may become stationary, or it may recede after the initiatory irritation has ceased to exist.

3. A precancerous state appears always to be interposed between the taking-effect of the cancer-inciting factor and the state of malignancy, so that in all probability there is no *direct* relation, if any, of the two events to one another as of cause and effect.

4. The primary irritant, the cancer-inciting factor, is not a "cause of cancer." There is no knowing whether the chronic condition which it may initiate under certain circumstances in the tissue, will ever mature into definite malignancy, or will not do so.

Conclusion. During the precancerous state the fate of the patient hangs in the balance. It is, therefore, of surpassing interest that the precancerous state appears perfectly amenable to curative intervention. There is no general rule for such intervention, and the multiplicity and infinite variety of conditions surrounding the precancerous state would require the separate consideration of each individual case for the determination of the therapeutic indications (Menétrier, p. 152[42]).

Of greater importance than to know how to treat an existing cancer would be the knowledge of how to prevent the development of a threatening cancer. Toward this end the precancerous state would seem to be the given point of attack.

Hence, location permitting, the clinical effort should always be directed toward recognizing a precancerous state, and then aborting or excising it, as the case may be.

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CARCINOMA OF THE ESOPHAGUS WITH ESPECIAL REFERENCE TO SITE.

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The following consists of a survey of 196 cases of esophageal cancer that have accumulated during the past ten years at the Cook County Hospital, and includes a detailed study of 51 cases that have come to necropsy. Ten of the latter serve as the basis of this report. Most of the larger studies of the pathology of esophageal cancer consist of collected case reports made for statistical or other purposes. The cases herein reported are those from under one hospital roof and were followed through from the admitting and examining room to the morgue.

Among 12,000 patients who in two months sought hospitalization or advice, there were 11 cases of cancer of the esophagus in a group of 59 cases of gastrointestinal cancer. There were 37 cases of cancer of the stomach. Stastistics as to the postmortem incidence of the

disease are not available. It appears, however, that they would be misleading, for the number of cases that came to necropsy seemed to be out of proportion to the number of cases of gastrointestinal cancer that were in the hospital. This was undoubtedly due to the interest in following up a case of hidden mediastinal tumor as opposed to one palpable in the abdomen.

The bifurcation of the trachea has been considered by many writers to be a very common site of esophageal cancer, and perhaps this is the prevailing notion. In the pathogenesis of the disease it has been repeatedly pointed out that the tumor may originate at the site of one of the constrictions, as where the gullet is crossed by the left bronchus. We have found carcinoma of the esophagus to be a very extensive disease; and believe that the same strange interest which has allowed authors to describe the disease anatomically, with possibly the etiological idea in the background, has helped to confuse the picture of the disease. The confusion and variances that one encounters in reviewing the literature reënforces the point, as the guilt of origin is ascribed to the upper, middle, or lower parts respectively.

A brief resume of some of the larger case reports may not be amiss. Huffel mentions 857 cases, in which it is noted that the middle and lower parts are involved in 699 instances. Wessel mentions 300 collected cases of Krauchaar in which the middle part was involved in 40 per cent of the cases. Petri finds in his own group of 44 cases the lower part affected in 18, the upper part 13 times. It is interesting to note in Lærche's statistical study that in a total of 1081 cases collected from the English literature, 430 were those of upper channel involvement; whereas in a total of 1084 cases from the German literature the reverse obtains, there being only 128 instances of upper esophageal disease. The same author quotes McKenzie as having made an observation of this same fact, namely, that the upper part of the channel appears to be the more frequent site of the tumor in the English speaking people, an observation that is not entirely unamusing.

In 33 of the 51 cases we were able to tabulate the up-and-down involvement of the channel to and from definite points, such as the cricoid cartilage or cardia. It might be worth while to call attention to an error that might readily be committed. In each case the 25 or 27 cm. of esophagus could be involved, a total of 825 cm. in 33 cases. (Cunningham, average length 25 cm.) Actually a total of 276 cm. (almost exactly one-third) are involved. We find that 25 cases, that is, 75 per cent involve some part of the 3 cm. segment which we have arbitrarily placed at 11, 12, and 13 cm. of the esophagus—area "X"; this seems far out of proportion but in reality is only a few per cent—about 8 too high, a deviation which is of no value in such a small number of cases. (Kindness of Dr. Ernest B. Zeisler).

In the acompanying chart the variation in the number of cases for each centimeter of esophagus is noted. The region of the bifur-

cation (11, 12, and 13 cm.) shows the most cases—25. But we must note that the mere extension of the tumor into a region does not prove that it originates there; as far as we know, only 1 case needs to have originated in area "X," for all of the other cases involve regions outside of "X." Thus the only really valuable cases for statistical studies are those of limited extent. The evidence does point toward some connection between carcinoma of the esophagus and the region "X;" either the growth originates more frequently in "X" or having originated elsewhere, it spreads more rapidly into "X" than into other parts. If this were a report on 3300, instead of 33 cases, we should not hesitate to conclude that one or the other alternatives is correct. We feel, however, that it would be as incorrect to say that the commonest site of origin is at the bifurcation as to say, if we might employ the homely analogy, that the night hours are the commonest ones for obstetrical labor, inasmuch as labor extending over so many hours must consume some at night.

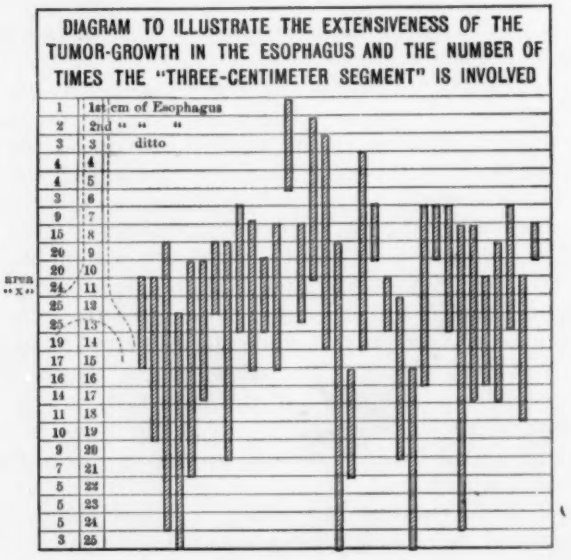
DIAGRAM TO ILLUSTRATE THE EXTENSIVENESS OF THE TUMOR-GROWTH IN THE ESOPHAGUS AND THE NUMBER OF TIMES THE "THREE-CENTIMETER SEGMENT" IS INVOLVED
1st cm of Esophagus
2nd " " "
ditto
AREA "X"

In 49 of the 51 necropsy cases there was an absence of metastases noted in 14 instances (28.5 per cent). Five of these showed a marked tendency to infiltrate the prevertebral tissues, aorta and others, and microscopic studies might have disclosed glandular metastases. There were widespread metastases to the viscera and glands of the abdomen in the 35 cases which disclosed metastatic infection. Of these the liver was involved 7 times, but always with mediastinal glandular or other visceral involvement. Petri in his group of 44 cases finds the liver to be the seat of metastatic tumor 6 times, but 4 of which involved the liver alone. Nirschl in quoting Colle's 15 cases finds the liver the seat in 6 cases, but in

only 1 was it involved alone. In the gross pathology mention should also be made of the associated vascular pathology. Tracheal or bronchial perforations exceed only a little those of aortic perforations, of which there are 4 cases. Regional thrombosis of the aorta and vena cava, respectively, were encountered in the 2 instances. In 6 other cases there was a marked fibrous union of the esophagus with the front wall of the aorta.

A pointed observation that may be made from our records is that the extensiveness of the involvement of the channel and the metastases and the duration of the symptomatology do not go hand in hand; but rather may be inversely proportional to one another. In 48 cases the average computed life history of the disease from the first complaint to the time of death is five and a half months. In 3 cases which had a clinical period of sixteen weeks, one-half of the channel was involved in an ulcerative carcinomatous process. In all but 1 there were metastases. But in those several instances where two-thirds or more of the channel was involved, it is to be noted that the duration of the disease was up to fifteen months. On the other hand, where the tumor is quite circumscribed and does not involve the channel for more than 3 cm., the duration of the symptoms was up to a year or more. There is, of course, nothing contradictory in these findings; the lack of tendency to spread explains the duration of the picture, except in those very few instances where the tumor was essentially obturating, and the patient was rapidly starved to death. We are led to conclude, however, that it is quite impossible to recognize the socalled early case, and that we know little or nothing about the extensiveness or rapid spread of the disease with the first complaints of the patient.

It is interesting to note that only 1 of the 51 cases that came to necropsy was a female; and of the group of 145 cases, only 10 were females. So low a percentage of females afflicted with the disease (5.6 per cent) we have not encountered in any series.

NOTE. Grateful acknowledgement is made of the courtesies extended by Dr. James G. Carr.

Summary. 1. Carcinoma of the esophagus is an extensive disease. In a series of 51 necropsies one-third of the esophagus was involved by the tumor growth.

2. Evidence that the disease begins at the site of the tracheal bifurcation is only presumptive. Only 1 case in this group needs to have originated there.

3. There is some relation between carcinoma of the esophagus and the region of the bifurcation. Either the growth originates there or spreads more rapidly into it.

4. It is quite impossible to recognize the so-called early case. At the time of the first complaint of the patient, there may already be extensive metastatic infection.

5. The average computed life history of the disease is five and a half months.

A FORM OF ACUTE HEMOLYTIC ANEMIA PROBABLY OF INFECTIOUS ORIGIN.

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During 1922 and 1923 there were admitted into this hospital three unusual cases characterized by sudden onset with elevation of temperature, leukocytosis, and a severe anemia resembling pernicious anemia, all of which symptoms promptly and rapidly disappeared following a single transfusion.

Reference to acute forms of pernicious anemia was made by Osler.[1] Elsner[2] mentions acute anemia of the pernicious type which may be due to syphilis, and other types in which the patients usually die within eight weeks. Krumbhaar[3] also writes of cases of acute hemolytic anemias which have recovered after a single transfusion. References to clinical descriptions of such cases, however, cannot be found. It hardly seems possible that cases similar to those described in this communication have not been reported. Perhaps they are obscured under unfamiliar terminology, and for that reason have not come to the attention of the writer. That the condition is not an infrequent one is evidenced by the fact that two other cases of like nature have been seen by the writer, and his attention has been called to three more treated in other hospitals.

Diseases in which rapidly progressing anemias of unknown etiology are the cardinal symptom are exceedingly uncommon. The hemolytic anemias, acquired and congenital, are characterized by hemal impoverishment, the establishment of which requires some length of time. Acute hemorrhage alone stands out as the condition which can bring about a very rapid blood loss, that is, in a period of hours or few days. Various authors trace the occurrence of acute unexplained anemias to syphilis, and to the unknown cause of pernicious anemia. In the latter disease an acute exacerbation may take place, with a sudden increase in the degree of anemia. The acuteness, however, is a question not of days but of weeks. A variety of hemolytic agents such as arsenic, mushrooms, snake venom, and blood with a high titer of hemolysin from an incompatible donor can cause sudden and voluminous erythrocytic destruction with consequent severe and prompt anemia. This is a well-known and easily recognized group.

The cases to be described present some differences from any previously described in the available literature. They resemble one another so closely that the writer believes it justifiable to classify

them for clinical purposes in one group. The outstanding features of the cases are the acuteness of the development of the symptoms, evidences of very rapid erythrocytic destruction, extreme regenerative action of the bone marrow, rapid recovery after therapy, and the absence of sequelæ. The case reports are as follows:

Case Reports. CASE I.—B. L., male, aged nineteen years, a student of pharmacy, using tobacco in small amounts; has always been perfectly well. There is no definite history of any previous illness. Up to the time of admission his complexion was ruddy.

Present Illness. Three days before admission, he was suddenly seized with right frontal headache and pain in the right eye, which continued. He became very weak and once he fainted. The color of his skin became yellowish. On admission his pulse was 104, the temperature 102° F.

Physical Examination. The patient is well nourished, not appearing acutely ill, his skin is of an icteroid tinge, and is pale and pasty. The scleræ are definitely icteric. His teeth show repair work, his gums are normal, the tonsils and pharynx are slightly congested. The lateral lobes of the thyroid are somewhat enlarged. The lungs are normal. Examination of the heart reveals a systolic murmur at the apex, probably hemic in origin. The abdomen is not distended. The liver is felt 2 cm. below the costal margin. The spleen is palpable 8 cm. below the costal margin, is rather firm, but not tender. No other abnormalities are noted.

On admission his general condition was very poor. He presented a yellowish-green appearance, and was very weak and apathetic.

His temperature on admission was 102° F. and ranged between that figure and 101° F. for six days, after which it gradually dropped to normal and remained so. The drop in the temperature followed the transfusion.

Examination of his eyegrounds disclosed moderate-sized superficial retinal hemorrhages, localized mainly about the discs. On April 20, the fasting contents of the stomach contained no free hydrochloric acid; forty minutes after a test meal free acid was present. Extractions obtained by the Rehfuss method on April 24 and 29 contained no free acid. The feces contained no blood, ova or parasites. The Wassermann reaction was negative, his blood chemistry showed a slight hyperglycemia (150 mgm. per 100 cc blood), the blood culture was sterile. The urobilin and urobilinogen outputs were as follows:

TABLE I.

1920.		Urobilinogen, dil. units.	Urobilin, dil. units.
April 12	Urine	2,000	2,375
14	Bile	8,575	13,636
20	Feces	104,000	240,000
24	Feces	6,400	7,200

The changes in his blood picture are depicted in Chart I and described in Table II. All the evidences of a profound anemia with every manifestation of hyperfunction of the bone marrow were seen. A very close resemblance to the blood in pernicious anemia during a crisis was noted. Red cells with mitotic, pyknotic, fragmented, degenerated and freshly extruded nuclei were found. Megaloblasts were easily demonstrated. A high degree of anisocytosis, poikilocytosis, numerous polychromatic cells, and cells with basophilic granulation (stippling) dominated the picture. Many free extruded nuclei were scattered throughout the preparation. A pronounced macrocytosis and microcytosis existed, and most of the cells appeared hyperchromic.

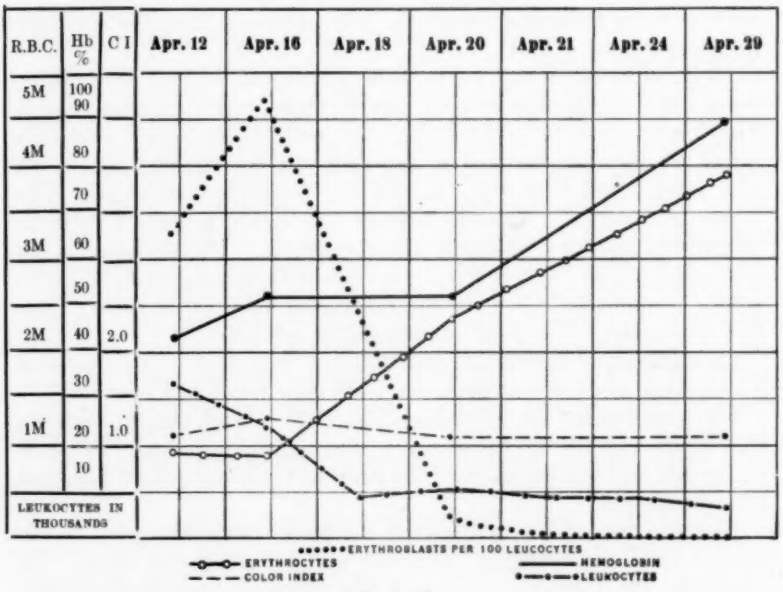

CHART I.

The great numbers of erythroblasts seen, made it apparent that the leukocyte count as estimated in the usual way was erroneous. Correction was therefore made by subtracting from the total number of cells per cubic centimeter as estimated from the white blood cell pipette, the erythroblasts as estimated in the stained preparations. Since this article was written, the author has found a description of a similar method used by N. Rosenthal in 1914.[4] The leukocytic picture betrayed evidences of active response to stimulation. The lymphocytes were but slightly increased in proportion to the myeloid cells. The latter showed in small quantities every type of cell associated with myeloid leukemia, some undifferentiated, and others in various stages of differentiation,

TABLE II

Date, 1922.	Hemoglobin, per cent (Dare).	Erythrocytes per c.mm.	Color index.	Platelets per c.mm.	Leukocytes per c.mm.	Polymorphonuclears.	Eosinophilia.	Basophilia.	Mononuclears.	Transitionals.	Lymphocytes.	Myeloblasts.	Neutrophilic myelocytes.	Basophilic myelocytes.	Metamyelocytes.	Normoblasts, per 100 leukocytes.	Megaloblasts, per 100 leukocytes.	Stained preparations.
April 11	...	...	...	...	...	55.5	0.5	...	8.0	2.0	24.5	7.00	2.5	...	8.0	63.5	3.5	Anisocytosis, poikilocytosis, polychromasia, stippling, hyperchromia and marked macrocytosis.
12	43	1,990,000	1.10	210,000	33,615	55.0	2.00	...	...	...	14.0	...	14.0	...	15.0	60.0	6.0	
					April 14, transfusion													
16	52	1,870,000	1.40	340,000	25,802	51.0	2.25	0.25	3.5	4.5	28.5	0.75	2.75	0.75	5.7	87.0	6.0	
18	...	...	...	...	8,381	48.0	2.00	0.08	...	...	40.1	1.00	7.90	...	0.9	44.0	5.0	
20	52	2,310,000	1.10	260,000	10,000	48.0	...	...	8.0	...	43.0	...	...	...	1.0	0	5.0	
21	...	...	...	...	7,400	52.0	1.00	...	3.0	...	44.0	...	...	...	...	0	1.0	Less than above.
24	...	...	...	...	7,400	35.0	1.00	...	6.0	...	58.0	...	...	...	...	0	0	
29	90	3,890,000	1.11	250,000	6,100	52.0	1.00	...	18.0	...	28.0	...	...	...	...	0	0	Slight amisocytosis and hyperchromia.

The lymphocytes, however, all appeared mature. These findings pointed to the stimulating action of some irritant, resulting in hyperfunction of hemopoiesis affecting the leukopoietic and erythropoietic elements equally. He rapidly grew worse, and after five days a transfusion of 350 cc of unmodified blood was given. The change in his condition was startling. He began to improve immediately, grew stronger, became brighter and quickly regained his normal status. The immature cells, both of the red and white series disappeared completely from the circulation within the five days following the initial and only transfusion. On discharge, no immature or developmental forms were found, there remained but a slight degree of anisocytosis and poikilocytosis and an appearance of hyperchromemia. Reëxamination several months later failed to show any evidence of disease. The blood examination was normal.

CASE II.—A. F., male, aged sixteen months, was admitted May 28, 1922. He was a perfectly normal child, always well except for an occasional slight cold. A doubtful history of having swallowed camphor some days before admission was elicited. Three days before admission he had three loose-bowel movements. In the evening he was restless and cried the greater part of the night; the next day his skin became yellowish in appearance, and the color rapidly deepened.

Physical examination shows a male child, well developed and well nourished. His skin is extremely pale and has a greenish-yellow tinge. The mucous membranes are blanched—they appear almost bloodless. The tonsils are enlarged. The lungs and heart are normal. The abdomen is slightly distended, the spleen edge is just palpable in the left flank.

TABLE III.

Date.	Hemoglobin, per cent (Dare).	Erythrocytes per c.mm.	Color index.	Leukocytes per c.mm.	Polymorphonuclears	Eosinophils.	Mononuclears.	Lymphocytes.	Erythroblasts per 100 leukocytes.	Stained preparations.
May 28, 1922	20	960,000	1.04	52,000	24	..	2	44	32	Transfusion.
29, 1922	30	990,000	1.50	32,200	50	..	..	50	0	Anisocytosis; poikilocytosis; marked macrocytosis.
30, 1922	35	1,450,000	1.20	18,400	43	6	6	45	0	
June 1, 1922	73	3,400,000	1.07	12,800	29	2	9	60	0	
July 17, 1924	65	5,720,000	..	12,200	44	3	1	52	0	Normal.

His temperature on admission was 100.8° F. but within about four hours rose to 103.6° F. The blood picture resembled that of

Case I. The anemia was much more profound, and evidences of regeneration were not as marked. Apparently the process was of much shorter duration, the insult to the reticulo endothelial system greater. His condition was so desperate (Chart II and Table III) that 120 cc. of unmodified blood were transfused on the day of admission, with the most gratifying result. Improvement was apparent at once, his temperature reaching a normal level within twenty-four hours, and three weeks after admission he was discharged well. He was brought back for reëxamination July 17, 1924, in perfect physical condition and with normal blood pressure.

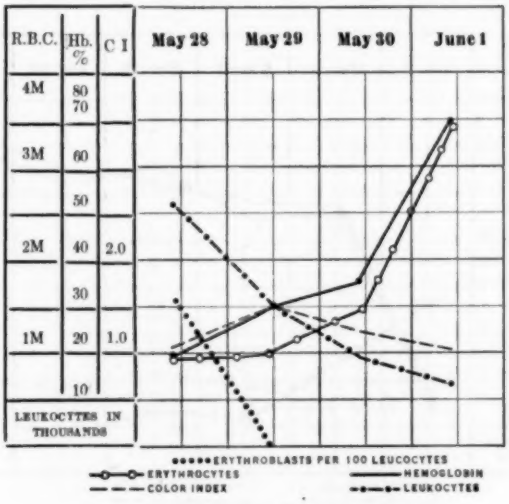

Chart II.

Case III.—L. B., female, aged thirty-five years, married, housewife, was admitted March 9, 1923. Her chief complaints were pain in the back, extremities, and head lasting six days. She was always well up to two years ago, when she was told she had a "leaky" heart. She suffered from dyspnea and palpitation on slight exertion, and also from car sickness. She had been married ten years, and had two children. Her menstrual history was normal. About two weeks before admission she suffered from an attack of what she thought was "grippe." She remained in bed for two or three days, with a temperature ranging around 101° F. When she left bed, she noticed pains in the back of a sticking nature, and dragging pains in the extremities. These pains gradually increased in severity until six days before admission, when she was compelled to return to bed. Her temperature at this time ranged between 101° F and 102° F. The next day she vomited, and the vomiting continued up to the time of admission. For the last

two or three days she had a cough. She noticed that her skin had become yellow.

Physical Examination. The patient appears acutely ill. She is fairly well developed and nourished. Her skin is pale and has a yellowish tint; the conjunctivæ are icteric. The teeth are in fairly good condition, the tongue is markedly coated, the throat is congested, the larynx negative. The apex of the heart is in the fifth intercostal space at 1.2 cm. ($\frac{1}{2}$ inch) outside the nipple line. There is a blowing systolic murmur over the apical area which is transmitted to the axilla and upward toward the base. The liver is palpable 2 cm. below the costal margin, the spleen is not felt.

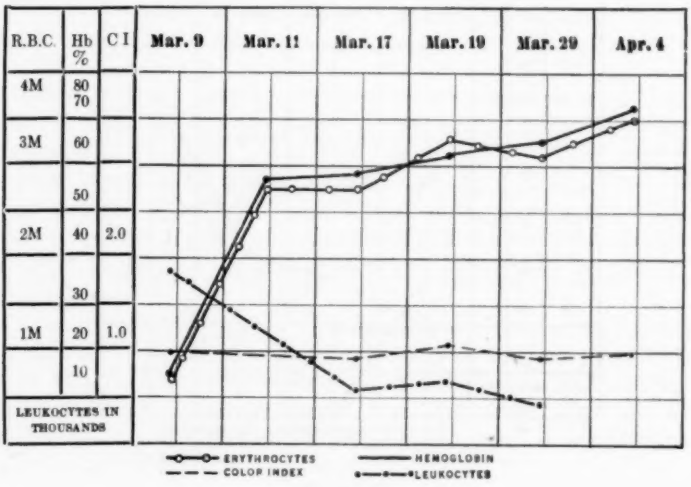

CHART III.

The temperature on admission was 102.4° F. The urine was negative except for a faint trace of albumin. The blood culture was sterile. The Wassermann reaction was negative. Examination of feces showed no ova or parasites.

The examination of the fundus showed conditions similar to those in Case I. Retinal hemorrhages were seen in both eyes, mainly in the regions of the discs.

Because of the profound anemia, immediate transfusion of 600 cc. of whole blood from a polycythemic patient (erythrocytes 12,000,000 per cc.) was done. Within twelve hours the temperature fell from 104° F. to normal, ranged about 101° F. for two days, gradually dropped to normal and remained there. The blood picture resembled that of Case I in all respects excepting in degree. The extreme erythropenia and leukocytosis were almost duplicates of Case II. The change in the blood picture after transfusion was similar (Chart III, Table IV). During convalescence she complained of

TABLE IV.

Date.	Hemoglobin, per cent (Dare).	Erythrocytes, per c.mm.	Color index.	Platelets per c.mm.	Leukocytes per c.mm.	Polymorphonuclears.	Eosinophils.	Basophils.	Mononuclears.	Lymphocytes.	Myelocytes.	Erythroblasts.	Stained preparations.
Mar. 9, 1923	14	780,000	0.95	150,000	37,000	81	...	...	2	10	7	Present	Anisocytosis transfusion.
11, 1923	55	2,800,000	0.97										
17, 1923	55	2,920,000	0.95	350,000	12,000	68	2	1	3	26	...	0	Slight anisocytosis.
19, 1923	65	3,100,000	1.05	...	12,900	73	...	...	3	24	...	0	
29, 1923	62	3,310,000	0.93	260,000	9,800	52	1	1	6	40	...	0	Slight anisocytosis and poikilocytosis.
April 4, 1923	70	3,640,000	0.96	...	...	...	...	...	...	...	...	...	
May 13, 1924	77	5,040,000	0.95	...	7,200	66	4	...	3	27	...	0	Normal.

persistent headache for which lumbar puncture was done followed by relief. Examination of the fluid showed no abnormalities. She was discharged well on April 16. She reported for reëxamination on May 13, 1924. Considering the previous cardiac condition, her status was normal and her blood picture was normal.

Comments. The onset was very sudden in 2 of the cases, a history of but three days' duration being elicited. In 1, the disease was ushered in with a slight diarrhea; in the second, with a severe headache. In the third instance, the onset was more complicated. Apparently she first suffered from pain in the back and extremities, thought to be of a "grippal" nature. The symptoms in all 3 instances were rapidly followed by weakness, pallor and slight icterus, and in 2 instances by vomiting.

Physical examination showed the patients to be intensely anemic, somewhat jaundiced and febrile. The spleens of 2 were palpable, but were not tender. In 2 there was definite hepatic enlargement. There was no bone marrow tenderness present in any of the cases. In 2 of the patients the eyegrounds revealed recent changes of a type commonly seen in pernicious anemia. Blood examinations revealed evidences of a profound anemia of a hyperchromic type and of an active myeloid production. At the time of admission a marked leukocytosis prevailed in all, being 52,000, 37,000 and 25,800 per c.mm., respectively, with a neutrophilic polymorphonucleosis of 81 per cent, 55 per cent and 51 per cent. In all cases the study of the erythrocytes showed changes indicative of a profound bone-marrow disturbance. All the associated changes present in severe pernicious anemia during a blastic crisis were observed. The number of normoblasts was enormous, in one instance amounting to about 3000 per c.mm. The fragility of the red cells was tested in the adults and was found to be normal.

The youth, being the first case admitted, was studied for several days, the transfusion being performed five days later. Before the transfusion, the course of the disease was steadily downward and a fatal termination seemed almost inevitable. Because of the favorable effect of the therapeutic measure adopted in this case and the grave condition of the 2 later cases, they were transfused within a few hours after admission with similar gratifying effects. The improvement in all was evident almost immediately, recovery was rapid and permanent, as proved by reëxaminations a year and two years later.

Thus, 3 cases similar in onset, symptomatology, course and response to treatment were observed. The anemia, which was the obvious outstanding, predominant, and the most alarming symptom, was due apparently to rapid blood destruction from either a bacterial or toxic agent. The evidence which points to infection as the cause, is the acute onset, temperature (not completely explain-

able by the anemia), leukocytosis, the enlarged spleen and possibly the specific effect of the transfusion. The latter did not produce benefit by replacement, since, in all the cases the enormous increase in the red cell content within the subsequent forty-eight hours cannot be so explained. The spleen, *per se*, apparently played only a secondary role in the hemolytic process, since the individuals were not anemic previous to this time and the enlargements promptly disappeared with recovery. In one instance, there was no demonstrable splenic enlargement. The cases closely resemble pernicious anemia in all ways excepting in the absence of previous history pointing to its existence, and in the complete recovery of the patients without sequelæ. The leukocytosis cannot be wholly accounted for by Minot's[5] explanation "When the marrow is working hard to form blood and is not succeeding well, it may be reflected in the blood picture of the white cells." This may explain the occasional high leukocyte counts and the few myelocytes that are sometimes seen during the course of pernicious anemia, but not the enormous leukocytoses and the relatively large numbers of immature cells present in these cases. There is no doubt that part of the leukocytosis is due to the compensatory effort of the bone marrow to replace the destroyed red cells involving at the same time the leukopoietic factor. However, a combination of factors offers a more satisfactory reason for the white blood picture. It is quite plausible that the exciting factor, probably infectious in nature, exercises a selective action on the cells of the reticulo endothelial system (hemolyto-poietic system of Krumbhaar.)[6] Naegeli[7] suggests that the hemolytic anemias are susceptible of that explanation. The reticulo endothelial system is made up of the productive, as well as the destructive components, of the hemopoietic structures. Therefore, a toxin acting as an irritating stimulus could well exert its influence on both components of this system with consequent increase of the blood destruction by a process of stimulation; similarly, this stimulant, affecting the bone marrow, would thus account for the appearance of the enormous numbers of immature and blastic cells of both red and white series. Furthermore, in the case of the red cell, destruction occurred more rapidly than production, resulting in a severe anemia. On the other hand, the destruction of the white cells apparently not being dependent on the reticulo endothelial system, and therefore not subject to the pathologic influence of the disease, proceeded at normal rates and resulted in a heaping up of fully developed and immature leukocytes in the circulation. In other words, the leukocytosis can be accounted for by three factors, infection, increased production, due to the stimulating action of the toxin, and heaping up. This explanation is offered as a tentative hypothesis to stimulate investigation along these lines.

The important practical point to be emphasized is the prompt

cessation of the pathological process after transfusion. To attempt to explain its action is purely speculative, but it acted as a specific in the 3 cases herein described and in 3 others to which the writer's attention has since been called.

Acknowledgment is expressed to the services of the late Dr. Leon Louria and Dr. W. K. Jacobs for permission to utilize the clinical material.

Conclusions. 1. Three cases, of a type hitherto undescribed in the available literature, characterized by sudden onset, fever, leukocytosis and severe anemia, are described.

2. Alterations in the blood, similar to those seen in pernicious anemia were found.

3. Evidences of rapid and enormous blood destruction were present.

4. The behavior suggests an infection with selective action concentrated on the reticulo endothelial system.

5. Prompt and permanent recovery followed a single transfusion of unmodified blood.

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CLINICAL VALUE OF SOME RECENT TESTS FOR LIVER FUNCTION.*

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We have made a comparative study of some of the newer and more promising tests for liver function. Our object has been to learn something of their relative value for diagnosis and prognosis and to find out, if possible, what tests are most helpful and best suited for the routine clinical study of cases with suspected or obvious liver disease. For this purpose, we used the Rowntree-

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Rosenthal test of dye excretion, the quantitative estimation of bilirubinemia by means of the icterus index as described by Bernheim[1] and the qualitative determination of bilirubinemia by the methods of van den Bergh and Fouchet.

Rowntree-Rosenthal Test. The liver function test now apparently receiving the greatest attention in this country is that of Rowntree and Rosenthal, based on the ability of the liver to excrete the dye substance, phenoltetrachlorphthalein, from the blood stream. Five milligrams of phenoltetrachlorphthalein per kilo of body weight are given intravenously and small specimens of blood are collected after fifteen minutes and again after an hour. The amount of dye in the serum of each specimen is then determined by colorimetric comparison. Normally from 3 to 5 per cent of dye is present in the blood serum at the end of fifteen minutes, and none at the end of an hour. With liver damage there is retention of the dye in the blood. Its estimation supposedly gives quantitative figures of the extent of impaired hepatic function.

Estimation of Bilirubinemia by Icterus Index. Recent work by Mann[2] and his co-workers has shown that the liver is not essential for the production of the bile pigment, bilirubin, and that a high percentage of it may be formed outside of the liver. But the liver is the sole excretory organ for this pigment in health, and upon this fact functional tests have been worked out by van den Bergh[3] and Meulengracht.[4] When bilirubin is not excreted by the normal channels through the liver it accumulates in the blood. Normally the quantity of bilirubin in the blood serum is small. The color of the serum deepens as the bilirubin increases. This occurs in certain cases of diseases of the liver and gall bladder, and in hemolytic conditions such as pernicious anemia and hemolytic jaundice. Blood serum is collected and compared in a colorimeter with an arbitrary standard, a 1 to 10,000 potassium bichromate solution. The standard solution is put in a 15-mm. cell and a reading is taken when the standard and the serum match. The standard number, 15, is then divided by the scale reading. If the color of the serum is too deep, it is diluted and the quotient is multiplied by the number of dilutions. Bernheim[1] found that in cases of clinical icterus the index was over 15, and when jaundice was absent it was below 15. As the normal range is between 2 and 5, latent jaundice is represented by figures between 6 and 16.

van den Bergh's Bilirubinemia Test. The van den Bergh qualitative test for bilirubinemia uses blood serum with Ehrlich's diazo mixture. There are two possible responses, a direct and an indirect. They supposedly differentiate between obstructive and nonobstructive jaundice, the latter arising from the direct injury to the liver cells or from jaundice of extrahepatic origin. In cases of obstructive jaundice, the color of the serum changes promptly from yellow to a pink or violet and indicates a positive direct

reaction. The direct reaction is negative in cases of nonobstructive jaundice. In the indirect van den Bergh reaction the serum is first treated with alcohol and some of the supernatant fluid is added to Ehrlich's diazo mixture. If the test is positive the pale yellow color of the serum changes to pink or violet as in the direct reaction of obstructive jaundice. The indirect reaction is positive in both obstructive and nonobstructive jaundice. Therefore, a blood serum showing a negative direct reaction but a positive indirect reaction is supposed to indicate a case of nonobstructive jaundice.

Fouchet's Bilirubinemia Test. In the Fouchet qualitative test for bilirubinemia a few drops of a reagent that oxidizes bilirubin are added to an equal amount of blood serum and mixed on a white porcelain surface. If hyperbilirubinemia is present to an extent of 1 to 60,000 or more, a green color develops which is specific for bile pigment. In normal serum bile pigment exists in a dilution of 1 to 600,000.

Clinical Results. In our series 173 patients were studied. Some had only part of the tests, but about half had all 4 tests done simultaneously one or more times. This group affords a basis of comparison of the relative clinical value of the various tests, though we will also report our results with the group in which only part of the tests were made.

Normal Control Cases without Liver Disease. There were 39 cases without suspected or proved liver damage. The icterus index was normal, (below 6) in all except 2, one a case of obesity, the other a case of pregnancy with moderately severe anemia. Rowntree-Rosenthal's dye test, done 16 times, was always normal. van den Bergh's bilirubinemia test, done 18 times, was negative in all except 2 in which the indirect reaction was weakly positive. Fouchet's bilirubinemia test in the same 18 cases was slightly positive in 3.

Cirrhosis of the Liver. Six cases of cirrhosis were studied, including 1 of syphilis of the liver and 1 of splenic anemia. The icterus index was increased in all except the case of splenic anemia, ranging from 9.3 to 23. Jaundice was uniformly present when the figures were 15 or over. Rowntree-Rosenthal's test showed a retention of the dye in the blood at the end of an hour in all except the case of splenic anemia, ranging from 7 to 15 per cent. Both the van den Bergh and Fouchet bilirubinemia tests were positive in varying degrees in all cases. One patient with cirrhosis, (Case I, Table I) a man aged twenty-nine years, had a rapid course and died four months after the onset. The retention of the dye in the blood varied little, being 12, 10 and 16 per cent, while the icterus index rose steadily from the first determination 10, to 45 shortly before death. Here the icterus index seemed to give a clue about the prognosis while the dye test did not. As the case of syphilis of the liver, (Case III, Table I) improved under treatment, the icterus-

index and the dye-retention figures both fell, and about equally. Before splenectomy, the case of splenic anemia, (Case VI, Table I) showed normal icterus-index and dye-retention figures. These results seemed to indicate good liver function and a favorable case for operation. At operation the liver appeared normal to inspection although slightly enlarged. Following operation the patient made a good recovery and has remained well nine months.

TABLE I.—LIVER CIRRHOSIS.

No.	Icterus index.	Percentage of dye in blood after		van den Bergh.		Fouchet.	Icterus.	Liver enlargement.	Remarks.
		15 min.	60 min.	Direct.	Indirect.				
I	10.7	12.0	10.0	+	++	++	0	+	Typical cirrhosis; died in 4 months.
	25.0	...	...	++	++	++	+	+	
	30.0	14.0	16.0	++	+++	++	+	+	
	30.0	...	...	++	+++	++	+	+	
	45.0	10.0	12.5	++	+++	++	+	+	
II	9.3	10.0	7.0	+	+++	+++	0	++	Typical cirrhosis; duration, 10 months.
III	12.5	7.5	9.0	0	+	+	0	++	Clinical picture of cirrhosis; Wassermann, ++++; ascites, ++; improved with arsphenamin.
	17.4	10.0	12.5	0	+	+	+	++	
	15.0	...	...	++	++	+	+	++	
	11.0	5.0	7.0	+	++	+	0	++	
IV	23.0	14.0	10.0	0	+++	+	++	++	Typical cirrhosis; repeated paracentesis; spleen enlarged.
	15.0	...	...	0	++	+	+	++	
V	15.0	...	...	...	...	..	0	+	Typical cirrhosis.
VI	6.0	5.0	0	0	+	+	0	++	Splenic anemia; no ascites; liver 5 cm. below costal margin.

Metastases in the Liver. Twenty-one cases of malignancy were studied in which there was a possibility of liver metastases. In 10, operation confirmed the diagnosis and demonstrated the presence or absence of extensive metastases. All cases (5) showing extensive metastases at operation had an increased icterus index, ranging from 8.2 to 157, and dye retention in the serum at the end of an hour, varying from 15 to 22 per cent. Here the dye test seemed the better indicator of the extent of liver metastases. The van den Bergh and Fouchet bilirubinemia tests were slightly positive when the icterus index was over 6 and strongly positive when it was over 10. In a general way the nonoperated cases gave similar results, though of course, the question of liver metastases could not be fully settled. The tests gave no help in detecting cases with slight liver involvement.

Catarrhal Jaundice and Acute Yellow Atrophy. These two conditions are grouped together because of the seemingly close relationship between them and because the tests promise help in their differentiation. The case of acute yellow atrophy, (Case VI, Table III) had an icterus index of 130 with strongly positive van den Bergh and Fouchet reactions. Unfortunately, a dye test was

TABLE II.—METASTASES IN THE LIVER. (OPERATED CASES.)

No.	Icterus index.	Percentage of dye in blood after		van den Bergh.		Fouchet.	Icterus.	Liver enlargement.	Remarks.
		15 min.	60 min.	Direct.	Indirect.				
I . .	8.2	13	15	++	++	++	0	+	Carcinoma of stomach; liver metastases, ++.
II . .	100.8	14	22	++++	++++	++++	++++	+++	Carcinoma of head of pancreas; liver metastases, ++++.
III . .	24.0	14	18½	++++	++++	++++	+	++	Carcinoma of pancreas; metastases, ++++.
IV . .	157.0	15	20	++++	++++	++++	++++	+	Carcinoma of head of pancreas; metastases, ++++.
V . .	72.0	18	22	++++	++++	++++	+++	++	Carcinoma of stomach; metastases, ++++.
VI . .	4.2	6	Tr.	0	0	0	0	+	Carcinoma of cervix of uterus; metastasis, none.
VII . .	3.8	5	0	0	0	0	0	0	Carcinoma of stomach; metastases, +
VIII . .	6.0	3	0	0	+	0	0	0	Carcinoma of stomach; malignant ulcer; metastases, none.
IX . .	3.6	4	0	0	0	+	0	0	Carcinoma of prostate; metastases, none.
X . .	6.0	5	0	0	+	+	0	0	Hypernephroma; metastases, none.

TABLE III.—CATARRHAL JAUNDICE—ACUTE YELLOW ATROPHY.

No.	Icterus index.	Percentage of dye in blood after		van den Bergh.		Fouchet.	Icterus.	Liver enlargement.	Remarks.
		15 min.	60 min.	Direct.	Indirect.				
I . .	115	..	..	++++	++++	++++	++++	0	Catarrhal jaundice.
	(4 days later)								
	30	..	..	++++	++++	++++	++	0	
II . .	105	20	20	++++	++++	++++	+++	0	Catarrhal jaundice; first tested after 5 weeks of jaundice.
	(8 days later)								
	62	14	20	++++	++++	++++	+++	0	
	(12 days later)								
	30.2	12	15	+++	+++	++++	++	0	
III . .	225	15	20	++++	++++	++++	++++	+	Catarrhal jaundice (malignancy suspected); operation with negative findings; first tested after 4 weeks of jaundice.
	220	20	18	++++	++++	++++	++++	+	
	(5 days after operation)								
	80	18	16	++	++	++	++++	+	
	(12 days after operation)								
	52	12	15	++	++	++	++	+(?)	
	(22 days after operation)								
	34	5	0	0	+	+	+	0	
IV . .	36	12	15	+++	+++	+++	++	0	Catarrhal jaundice.
	(8 days later)								
	16	12	12	0	+++	++	+	0	
V . .	151	..	..	+++	+++	+++	++++	++	Catarrhal jaundice.
	93	..	..	++	++	++	++++	++	
	28	..	..	0	++	+	++	+	
VI . .	130	..	..	++++	++++	++++	++++	0	Acute yellow atrophy; necropsy.

not made. Seven cases of catarrhal jaundice had icterus index figures ranging from 225, (the highest obtained) during the height of the disease, to 16 during the stage of decline. Serum dye retention varied from 20 per cent to none at the end of an hour, according to the stage of the disease. Results with the van den Bergh and Fouchet tests declined from very strongly positive reactions to negative as the condition cleared up, the indirect van den Bergh positive reaction being the last to disappear. Dye retention declined more slowly during convalescence than the icterus index, and would seem, therefore, to be of less value than the latter in differentiating severe catarrhal jaundice from malignancy or acute yellow atrophy. One case of catarrhal jaundice of five weeks' duration (Case II, Table III), for example, was thought at first to be a possible malignancy. The dye retention in the serum remained about the same, but a rapid fall in the icterus index before the intensity of the jaundice diminished or the stools showed bile, was the first indication that we were dealing with a benign form of jaundice. Another case of catarrhal jaundice of four weeks' duration (Case III, Table III) was operated upon for possible malignancy with negative findings. A few days later the icterus index fell rapidly and the patient went on to an uneventful recovery. Had there been a delay until the icterus index had dropped, the operation might have been avoided.

TABLE IV.—CARDIAC DECOMPENSATION (8 CASES).

No.	Icterus index.	Percentage of dye in blood after		van den Bergh.		Fouchet.	Icterus.	Liver enlargement.	Remarks.
		15 min.	60 min.	Direct.	Indirect.				
I . .	129.0	8	12	+++	+++	+++	+++	+++	Mitral; fibrillation; died in 1 month.
II . .	10.0	10	9	0	+	0	0	+++	Mitral; anasarca; marked improvement.
III . .	10.2	5	0	0	+	0	0	+++	Syphilitic aortitis; marked improvement.
IV . .	18.7	5	0	0	+	0	+	+++	Mitral and tricuspid; died in 7 weeks.
V . .	10.0	..	..	+	+	+	0	+++	Valvular disease; anasarca; died in 10 days.
VI . .	22.0	5	7	++	++	++	+	+++	
	30.0	..	..	+++	+++	++	+	+++	Valvular disease; fibrillation; died in 2 months.
VII . .	5.0	5	0	0	0	0	0	+	Arteriosclerosis; coronary disease; died.
VIII . .	8.8	6	0	+	+	+	0	+++	Valvular disease; fibrillation; moderate improvement.

Passive Congestion of the Liver from Cardiac Decompensation. Mild degrees of a jaundice and liver enlargement are rather common in cardiac decompensation. In 15 such cases, the icterus index seemed to follow rather closely the degree of cardiac decompensation. Cases with little or no decompensation all had figures below 8.

All cases with index figures above 16—4 in this series—died within two months. Two cases with slightly enlarged livers but no icterus returned normal figures though the prognosis was apparently quite poor. Our findings in general, therefore, agreed with those of Bernheim[1] who found that the icterus index was of value in determining the prognosis and the degree of decompensation.

Dye retention did not seem to follow very closely increases in the icterus index. We were unable to establish any definite relationship between either degree of decompensation or prognosis and dye retention. van den Bergh and Fouchet bilirubinemia determinations were usually positive in varying degrees as the icterus index increased above normal. A study of our results with the four liver function tests made us feel that the icterus index alone promises some help in determining the degree of decompensation and prognosis in advanced cases of cardiac decompensation.

TABLE V.—CHOLECYSTITIS; CHOLELITHIASIS.

No.	Icterus index.	Percentage of dye in blood after		van den Bergh.		Fouchet.	Icterus.	Liver enlargement.	Remarks.
		15 min.	60 min.	Direct.	Indirect.				
I	10.5	5	0	0	+	0	0	0	Cholecystitis (operation).
II	8.7	6	0	0	++	+	0	0	Cholecystitis (operation).
III	(During attack)								
	16.2	5	0	+++	+++	+	+	0	Cholecystitis; cholelithiasis (?).
	(3 days later)								
	6.7	..	..	0	+	+	0	0	
IV	14.0	..	..	0	++	0	0	0	Cholecystitis, following attack.
V	144.0	15	20	++++	++++	++++	++++	+	Cholelithiasis (operation) adhesions about ducts.
	187.0	..	..	++++	++++	++++	++++	+	
	(6 days after operation; 1 day before death)								
VI	6.8	5	0	0	+	0	0	0	Gangrenous gall bladder, with stones (operation).
VII	12.5	5	0	0	+	+	0	0	Cholelithiasis (operation).
	(10 days after operation)								
	4.6	..	..	....	0	0	0	0	
VIII	12.6	6	0	0	++	+	0	0	Cholecystitis (operation).
	(18 days after operation)								
	6.0	..	..	0	0	+	0	0	

Cholecystitis and Cholelithiasis. Thirty-seven cases of biliary tract disease were studied. The diagnosis was verified by operation in 24. All cases with jaundice showed icterus-index figures over 15. All the rest operated upon, (19) returned figures in the zone of latent jaundice (6 to 16) except 1. As reported by Bernheim[1] we feel that the icterus index has its greatest value in this group of cases. The only confusion that may arise, apparently, is that duodenal ulcer usually gives figures in the zone of latent jaundice; 9 out of 10 cases of duodenal ulcer in our series did this. But other methods such as roentgenographic study usually meet this difficulty. After operation and recovery the icterus index always returned to normal. With the dye test we had hoped to obtain some evidence

of impaired liver function in the hepatitis that is supposed to accompany biliary tract disease. In this we were disappointed as all cases without jaundice returned normal dye figures. Four cases with common-duct obstruction showed dye retention after one hour varying from 8 to 20 per cent. This test we believe is valuable in determining the ability of the liver to withstand the shock of operation. The van den Bergh test in this group served only to verify that the increased figures of the icterus index were due to hyperbilirubinemia. Fouchet's test for bilirubinemia we found, as Garvin[5] recently reported, to be quite unreliable, frequently being negative in proved biliary tract disease.

Arsenical Hepatitis. Schamberg and Brown[6] suggested "that the serum-bilirubin determination be made from time to time in patients receiving arsenical therapy as a guide to the toleration of the drug by the liver." They pointed out that it might be wise to interrupt arsenical treatment in syphilis when the serum bilirubin became higher than normal. The only case of arsenical hepatitis in our series was a woman who developed jaundice after receiving 18 injections of an arsenical. The icterus index figure during the jaundice stage was 30, but remained high, (11.2) four months after the jaundice had disappeared. Here it seemed unwise to resume the treatment until the index became normal. It is interesting to note that the serum dye test was normal both times it was done in this case.

Discussion. A careful study of our results with the icterus index and the dye retention test failed to show any uniform close agreement between them. With few exceptions cases of apparently marked impairment of liver function gave positive results with both tests. In 2 cases of cirrhosis and in some of the cases of metastatic liver carcinoma, the dye test seemed better than the icterus index in giving evidence of the degree of liver involvement. However, in every instance in our series in which there was a positive result with the dye test, the icterus index was also increased above normal. Some of the cases with low-grade jaundice, and most of the cases with latent jaundice, gave normal results with the dye test in striking contrast to the increased figures with the icterus index. There were no false positive results with the dye test. In 10 cases out of 173 we obtained increased figures for the icterus index without any adequate explanation. It is interesting to note that all cases of pernicious anemia examined (6) had an increased icterus index and normal dye test, while all cases of secondary anemia (14) had a low icterus index, thus confirming similar previous observations.

Our results have given us the impression that the icterus index is the most useful single liver function test that we have. The dye test seems to be of supplementary value in estimating liver function. The van den Bergh qualitative test distinguishes between obstructive and nonobstructive jaundice and helps to detect any false positive results with the icterus index, as it is a specific qualita-

tive test for bilirubin. The advantages which the icterus index has over most of the other functional liver tests, and especially over the dye test, are that it is simpler, easier to perform and less objectionable to the patient. Maurer and Gatewood[7] have recently reported 3 deaths in patients two to seven days after the Rowntree-Rosenthal dye test was made. If it should be shown by other observers that such deaths are due to the administration of the dye it would impose a very serious limitation on its use in clinical medicine. However, the dye has been used by a large number of other workers, and as far as we can learn none of them report any serious development. In our series of 82 dye injections, induration of the vein at the site of injection occurred seven times and a chill twice. No toxic effects were observed.*

Conclusions. 1. The Fouchet test proved unreliable in our hands for detecting minor grades of bilirubinemia. In other respects the van den Bergh test served very well in its place.

2. The van den Bergh test has distinct value in studying liver function and jaundice. Positive results with both reactions indicate impaired liver function, but the extent must be determined by the icterus index or dye test. It helps as a specific qualitative test for bile pigment to control readings of the icterus index in the zone of latent jaundice. It distinguishes between hemolytic and obstructive jaundice.

3. Our study would seem to indicate that the icterus index is the most useful single functional liver test that we have for clinical work.

(*a*) It is easily and quickly performed, unobjectionable to the patient and free from danger.

(*b*) Its greatest value is in the diagnosis of cases of cholecystitis and cholelithiasis without clinical jaundice.

(*c*) It is a distinct aid in distinguishing between obstructive jaundice due to malignancy and catarrhal jaundice by showing whether the jaundice is increasing, diminishing or stationary.

(*d*) It is helpful in the diagnosis of cirrhosis and malignant metastases in the liver, though apparently less so than the dye retention test.

(*e*) It may indicate the degree of cardiac decompensation.

(*f*) It serves as a guide to the toleration of the liver to arsenicals in the treatment of syphilis.

(*g*) It will determine whether obstructive jaundice has been relieved by operation.

(*h*) It helps to differentiate the primary from the secondary anemias.

* Quite recently Rosenthal[8] reported a new dye substance, bromsulphalein. This, he states, is safe and nonirritating, and expresses directly the degree of impaired liver function by the percentage present in the blood serum thirty minutes after injection. As yet it has had no general clinical application.

4. The Rowntree-Rosenthal dye test is of supplementary value in measuring liver function. For clinical work it is more complicated, more objectionable to the patient and may not be entirely free from danger.

(*a*) It seems to be of greater value than the icterus index in the diagnosis of cirrhosis and malignant metastases in the liver.

(*b*) In surgical cases with jaundice, the dye test helps to determine the degree of damage to the liver parenchyma and hence the surgical risk, and acts as a guide to the operative procedure to be undertaken.

(*c*) Its greatest value apparently is in the diagnosis of liver disease in patients without jaundice. Here a positive result points to liver involvement, a negative result helps to rule it out.

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FURTHER CLINICAL AND OPERATIVE STUDIES OF THE ICTERUS INDEX.

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Liver function study at present is a virile clinical subject. During the past few years there has been real progress in the development of laboratory tests of liver activity. Each of the three best known liver functions has been called into service to answer for

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the actions of the other two. Clinical experience has shown that while these three functions are probably very closely related, they may act entirely independently of each other. For example, the glycogenic function may not be influenced by the liver's inability to detoxicate proteins; and likewise, the bile-forming power of the liver may not be dependent on either of the other two. These three functions undoubtedly modify the activity of every other essential organ in the body. Therefore, every functional liver test must be interpreted in the light of the liver's influence on other organs and also the influence of other organs on the liver. There are probably still other functions. For example, the liver may exert a powerful influence on the blood-forming organs whose action in turn may certainly affect the liver.

Realizing our inability to test every function, we are convinced that certain comparatively simple tests give us much clinical help in those diseases in which liver pathology is concerned. We have endeavored to study the liver's inability to detoxicate proteins by Widal's hemoclastic crisis method. We have derived much clinical help from a study of the liver's ability to form bile and to eliminate bilirubin from the blood stream. In this study we have utilized the quantitative colorimetric method developed in the laboratory of the Lenox Hill Hospital, New York, by their chemist, Dr. Adolph Bernhard, and by Dr. H. Peter Maue,[1] following the suggestion made by Dr. De Witte Stetten.[2] The above group of workers gave us the very usable term "icterus index" which was later adopted by Bernheim,[3] ourselves,[4] and others. We have used the technic as given in the footnote* below and find it simple and producing very slight variation in the hands of different technicians.

This additional report is given to emphasize the benefits derived from this test in everyday practice of medicine and surgery. The quantitative serum bilirubin test or icterus index as recently reported by O'Leary[5] from the Mayo Clinic, practically parallels the much more complicated phenoltetrachlorphthalein test of Rosenthal. The later technic requires the withdrawing of 10 cc. of blood at four different intervals, the intravenous injection of a possibly harmful dye, and a specially constructed colorimeter unsuitable to any other use. We feel that valuable as the dye tests

* Three or 4 cc. of blood are withdrawn from a vein. The blood, kept away from the light, is allowed to clot and is then centrifugalized. The supernatant serum is removed with a pipette and compared in a calorimeter with an arbitrary standard —a 1 to 10,000 potassium dichromate solution (0.05 gm. to 500 cc. of distilled water). This solution is paler than normal serum. The Bock-Benedict colorimeter which requires less serum than the Duboscq type is the one that was used in these tests. The standard solution is put into the 15-mm. cell. The reading is taken at the point on the scale at which the serum and standard match. The standard number, 15, is then divided by the scale reading. The quotient is the icterus *index*. For example: If the scale reading is 3 the index is 5. If the color of the serum is too deep it is necessary to dilute it with a 0.9 sodium chlorid solution. The quotient is then multiplied by the number of dilutions. For example: If the number of dilutions is 10 the index in the foregoing instance would be 50.

may be, they are still too impractical for the great mass of clinicians who need to utilize liver-function tests. Judging from the untoward results already reported, the general use of the dye tests will soon result in their general disuse. Bloom[6] and Rosenau conclude that the use of phenoltetrachlorphthalein dye will produce a positive van den Bergh in a normal person within sixty minutes. Following their tests, 14.8 per cent of their patients developed thrombosis at the site of injection; 22.2 per cent, local reactions; and 7.4 per cent, chills. A total of 37 per cent showed untoward reactions. After careful use of phenoltetrachlorphthalein for the detection of impairment of liver-cell function, Maurer, Siegfried and L. C. Gatewood[7] were convinced that the injection of substances of this group is not without danger. We do not wish to condemn the dye tests *in toto* or even at all if in the hands of workers who can report such results as Graham[8] and Sherwood Moore.[8] However, before using such tests profusely, it is well to be familiar with the works of the above quoted authors, to which group, I desire to add the recent work of Ottenberg and Abramson[9] showing the certain and extensive liver lesions when overdoses of the dye are used experimentally.

In the effort to correlate the known functions of the liver with the clinical observations, we have of necessity noted a close concurrent relation to the behavior of the blood-stream leukocytes. We have shown previously[4] that a bilirubinemia in typhoid fever is as constant as a leukopenia. Further, Livingston and Squires[10] have shown from the Bellevue Hospital records that even typhoid perforation results in a leukocytosis in only 15 per cent of their cases, and in most of these cases, there was some other pyogenic complication. When perforation occurred at any time during the first three weeks, there was no leukocytosis at all. It is our belief that during this period the liver is then carrying its greatest strain and that its cells, unsensitized to the typhoid toxin, are in a state of protein shock. The proteopexic function of the liver is most disturbed and probably the sensitization of the cells has not yet taken place completely. At this period the shock is more in the nature of a nonspecific protein reaction. In this way, we can see a relationship between the clinical state on the one hand and these liver function tests on the other. We believe that a study of the proteopexic function in relation to the bile or bilirubin function of the liver will correlate such tests as quantitative bilirubinemia and dye elimination[11] with the hemoclastic shock.

When these two tests, carefully made, do not agree, then different functions of the liver are disturbed clinically. They have a right to differ at times, for their factors, though related, are variables. Realizing that the two tests show two different though related functions of the liver, we can see a closer relation of greater clinical value in the tables of Piersol and Bockus.[11] They interpret their charts in favor of the dye tests and to the disadvantage of the hemoclastic

TABLE I.—OPERATIVE CASES.

No.	Patient.	Icterus index.		Proven diagnosis.	Remarks.
		Before.	After.		
5	Mr. S.	8.5	4.0	Acute cholecystitis with chronic cholelithiasis	Acute infection of old condition; hepatitis modified.
7	Mrs. Y.	15.0	6.0	Vincent's angina, severe	Was icteric then; died 4 months later from cerebral hemorrhages; hepatitis.
8	Mr. O.	8.0	4.0	Chronic appendicitis with colitis and adhesions	There had been some nausea and bowel hemorrhages; light hepatitis.
9	Mrs. H.	7.4	5.0	Chronic cholecystitis and adhesions	Moderately toxic hepatitis.
10	Mrs. W.	11.5	4.0	Chronic cholecystitis and cholelithiasis	Definite hepatitis.
11	Mr. M. E.	15.4	6.0	Chronic duodenal ulcer with adhesions around gall bladder	Severe hepatitis, toxic.
13	Mrs. H.	13.5	5.1	Chronic appendicitis and colitis with gall bladder and colon adhesions; blocking	Toxic hepatitis.
14	Mrs. F.	8.8	5.0	Chronic colitis with adhesions	There was nausea and hepatitis.
15	Mrs. H.	6.8	5.0	Duodenal and hepatic flexure with adhesions	There were severe toxic nervous spells.
16	Miss F.	9.5	4.0	Chronic gall bladder and appendix	Severe toxic spells.
17	Mrs. B.	7.2	4.0	Chronic appendicitis with colitis	No evidence of hepatitis.
18	Mrs. C.	8.2	5.0	Chronic appendicitis with duodenal adhesions and chronic gall bladder	The toxemia was moderate.
19	Mrs. L.	15.1	7.0	Colon adhesions up to mid-transverse colon	Dizziness during attacks severe; after operation, completely relieved.
22	Mrs. H.	12.2	6.0	Chronic appendicitis and cecal and hepatic flexure; adhesions of gall bladder	Very much evidence of hepatitis.
23	E. W.	20.0	7.0	Chronic cholecystitis and hepatitis	*Had acute exacerbations.*
24	Mr. M.	18.0	7.2	Chronic appendicitis and cholecystitis	Before operation, 11.5; after anesthetic, 13.5; postoperative, 13.5; 4 days later, 17.4; 21 days later, 8.8; 12 hours after transfusion index was 39.5 and heart nearly failed.
26	Mrs. L.	26.6	7.0	Chronic cholecystitis	Severe hepatitis.
27	Mr. S.	12.5	7.0	Chronic appendicitis and pernicious anemia and duodenal adhesions	
33	Mrs. S.	8.8	5.0	Chronic gall bladder and stones with adhesions	
38	Mrs. P.	8.7	6.0	Chronic appendicitis with adhesions; dermoid of uterus; psoriasis	
43	Mrs. M. A.	15.0	6.4	Chronic cholecystitis and stones	Early attacks, 15; 1 day postoperative, 13; 5 days postoperative, 8.3; 16 days postoperative, 6.4.
37	R. G.	12.0	6.0	Duodenal adhesions	Mental depression; hepatitis.

crisis because they emphasize the dye or bilirubin eliminative function as of greater value than the protein detoxication function. These functions are undoubtedly correlated and probably inseparable. The above authors[11] found the dye retention was very high when the icterus was very intense, but the degree of dye retention did not parallel the intensity of the jaundice. When the dye retention was great, urobilin was present in the urine, but it was absent when the dysfunction was slight. These observations would seem to favor the quantitative bilirubinemia determination or icterus index, as the test of choice among those in use at the present time. New dyes are being tested by Rosenthal and White.[12] A simpler technic and a less toxic dye may bring this test into greater clinical usefulness than any previously reported.

On the previous page we have given our tabulation and study of a considerable group of cases not previously recorded. The first group consists of 22 cases on which a liver dysfunction was definitely diagnosed preoperatively. There was an operative necessity in each case. The average preoperative icterus index was 12.3 and the postoperative index was 5.5. Operation confirmed every diagnosis.

The operative cases in which the index was 6 or below were grouped. The average preoperative index was 5.7 and the postoperative index was 5.3. In no case was there any suggestion of a hepatitis. The absence of liver or gall bladder disease could be checked from any of our three sources of diagnosis, namely, icterus index, clinical observations, or operative findings.

TABLE II.—OPERATED CASES, ICTERUS INDEX 6 AND BELOW—NO HEPATIC DISEASE SUSPECTED.

No.	Patient.	Index.		Proven diagnosis.	Remarks.
		Before.	After.		
1	Mrs. C.	6.0	6.0	Chronic appendicitis and colitis with adhesions	No hepatitis; arthritis.
2	Mrs. T.	6.0	6.0	Chronic appendicitis and chronic nephrolithiasis	Toxic, but no hepatitis.
3	Miss D.	7.0	6.0	Twisted ped., 1st; acute intestinal obs., 2d	No reason to suspect liver damage.
4	B. M. S.	6.0	6.0	Gastric adhesions about old gastroenterostomy	No blocking of bile ducts.
6	Mrs. Y.	4.3	4.3	Chronic appendicitis and colitis	No hepatitis.
12	Mrs. M.	5.0	5.0	Chronic appendicitis	More pain than toxemia.
31	Mrs. Z.	5.4	5.0	Chronic appendicitis with adhesions, not obstructing	No hepatitis.
32	Mrs. H.	5.8	5.0	Chronic appendicitis with adhesions	Eyes disturbed.
121	Miss H.	6.0	5.0	Colon adhesions	No hepatitis.

A group of 18 cases could be classed as toxic by the symptoms of migraine, biliousness, severe dizziness, and toxic convulsions. All these cases carried intestinal protozoa. Their average counts were: Leukocytes, 6500; neutrophils, 57 per cent; mononuclears, 43 per cent; icterus index average was 13.4. Improvement of the condition invariably was accompanied by a lowered index.

TABLE III.—TOXIC CASES.

Case.	White blood cells.	Icterus index.	Neutrophils.	Mononuclears.
P.	7200	12.5	43	57
M.	6400	9.0	51	49
M. C.	7800	15.0	56	41
B.	7000	15.0	55	45
M.	8800	19.0	71	29
P.	6200	8.0	58	42
D. B.	5800	15.0	58	42
Mrs. L.	5800	10.0	65	35
B.	7100	15.0	71	29
N. R. W.	3600	16.0	61	39
H.	6000	18.5	67	33
H.	6600	12.2	60	40
M.	6100	20.0	56	44
Ma.	6000	5.0	56	44
H.	5200	5.8	57	43
C.	6600	20.0	56	44
Co	7500	12.5	56	44
H.	7800	18.0	43	57

Table IV represents a small group where a toxic hepatitis was undoubtedly present clinically. There were 6 cases with an average index of 14.9. Operation proved the diagnosis in every case.

TABLE IV.—HIGH INDEX WITH HEPATITIS ALONE—AND TOXEMIA.

No.	Patient.	Index.		Reasons.
		Before.	After.	
7	Mrs. Y.	15.0	7.2	Vincent's angina,
11	Mr. M. K.	15.4	5.6	Duodenal ulcer with adhesions.
13	Mrs. H.	13.5	5.1	Adhesions about duodenum and chronic appendicitis.
19	Mrs. L.	15.0	7.0	Adhesions cecal and flexural.
24	Mr. M.	18.0	7.0	Appendicitis and gall bladder.
37	R. G.	12.0	6.0	Appendicitis and duodenal adhesions, mental.

The index in the appendicitis and mild colitis cases averaged 6.5 as proven by operative procedure.

There were 9 cases in which the gall bladder was definitely infected in such a way as to give either a blocking or an ascending hepatitis. The average preoperative index was 13.5 and the postoperative taken from two to three weeks later was 5.5.

TABLE V.—INDEX, WITH GALL BLADDER DEFINITELY INFECTED—CHRONIC.

No.	Patient.	Index.		Diagnosis.
		Before.	After.	
5	Mr. S.	8.5	4.0	Acute cholecystitis.
10	Mrs. W.	11.5	4.2	Chronic and acute cholecystitis.
16	Miss F.	9.5	6.0	Chronic cholecystitis and appendicitis.
23	W.	20.0	7.0	Chronic and acute cholecystitis.
24	M.	15.0	7.0	Appendicitis and cholecystitis.
26	L.	26.6	7.0	Chronic cholecystitis.
33	Mrs. S.	8.0	5.2	Chronic cholecystitis and colitis.
43	Mrs. M. A.	15.0	5.0	Chronic cholecystitis with stones.
9	Mrs. H.	7.5	5.0	Chronic cholecystitis.

There were 42 nonoperative cases in which the symptoms, physical findings, history and roentgen ray would definitely diagnose liver and gall bladder disease. The average icterus index was 13.8 in this group.

TABLE VI.—NONOPERATIVE CASES IN WHICH SYMPTOMS AND ROENTGEN-RAY POINT CLEARLY TO GALL BLADDER AND HEPATITIS.

No.	Patient.	Index.	Diagnosis.
28	Mr. J.	9.6	Cholecystitis and hepatitis.
39	Mrs. C.	20.0	Hepatitis, cardiac.
41	Mr. L.	18.0	Amebic hepatitis.
42	Mrs. C.	12.5	Amebic hepatitis.
46	Miss H.	8.6	Colitis and gall bladder, hepatitis.
49	P. P.	18.0	Cholecystitis.
55	Mr. L.	12.0	Cholecystitis.
58	Mr. W.	11.2	Hepatitis.
61	Mr. Wi.	11.2	Hepatitis and appendicitis.
62	Mrs. P.	12.5	Hepatitis, colitis and arthritis.
63	Mr. M.	9.5	Hepatitis and gall bladder.
67	Mrs. M. C.	15.0	Hepatitis and lues.
68	Mrs. B.	15.0	Hepatitis and gall bladder.
69	J. M.	19.0	Hepatitis and polycythemia.
70	Miss R.	18.0	Cholecystitis.
71	Mr. T.	18.0	Cholecystitis.
75	Mrs. P.	8.0	Hepatitis and appendicitis.
79	Mr. G.	13.8	Hepatitis and duodenal ulcer.
85	J. P. C.	18.0	Hepatitis and colitis.
89	Mr. O.	10.0	Amebic hepatitis.
90	R. P.	22.5	Cholecystitis.
92	Mrs. A.	7.5	Hepatitis and colitis.
93	Mr. Z.	13.8	Hepatitis and gall bladder.
94	Mr. T.	15.0	Hepatitis.
96	Mrs. B.	8.4	Hepatitis and duodenal ulcer.
97	Mrs. B.	7.5	Hepatitis and iritis.
98	Mrs. D. B.	15.0	Hepatitis and cholecystitis.
100	Miss H.	18.0	Hepatitis and cholecystitis.
101	Miss P.	22.0	Hepatitis and cholecystitis.
102	Mrs. B.	7.0	Hepatitis and cholecystitis.
104	Mr. W.	8.6	Myocarditis.
105	Mrs. L.	10.0	Hepatitis.
108	Mr. B.	15.0	Hepatitis and cholecystitis.
109	Mrs. N. R. W.	16.0	Hepatitis and cholecystitis.
110	Mrs. G. O. M.	10.0	Liver abscess.
111	Mr. N.	22.5	Hepatitis and iritis.
112	Mrs. P.	10.0	Hepatitis and enteritis.
115	Mr. O. M. T.	16.0	Hepatitis and gall bladder.
116	Mrs. S.	10.0	Hepatitis and fibroid.
117	Mr. P.	30.0	Cholecystitis.
118	Mr. H.	15.0	Hepatitis and iritis.
119	L. M. D.	6.0	Hepatitis and gall stones.

Of 43 nonoperative cases whose symptomatology, history and physical findings did not point to liver disease the average index was 5.8 The average here was increased by a few cases having more than usual colon symptoms.

TABLE VII.—NONOPERATED CASES IN WHICH NO HEPATIC OR GALL-BLADDER DISEASE IS SUSPECTED.

No.	Name.	Index.	Diagnosis.
29	Mrs. L.	6.2	Arthritis and appendicitis.
30	Mrs. F.	3.4	Arthritis and appendicitis.
34	Mrs. M. C.	5.2	Tuberculosis.
35	Mrs. C.	5.6	Chronic bronchitis and colitis.
44	Mr. H.	8.6	Chronic appendicitis.
45	Mrs. M. L.	10.0	Chronic colitis.
47	Miss C.	7.5	Colitis.
48	Mr. A.	7.5	Gastric ulcer.
50	Mrs. R.	5.0	Chronic appendicitis.
51	Mrs. S.	5.2	Chronic colitis.
52	Mrs. T.	4.0	Chronic colitis.
53	E. T. D.	5.0	Lues.
54	J. M. S.	4.0	Lues.
56	Miss Bl.	6.0	Chronic appendicitis.
57	Miss B.	7.5	Colon stasis.
59	Mrs. M.	5.0	Chronic colitis.
60	Mr. J.	5.0	Gastric ulcer.
64	Mrs. B.	3.0	Psychosis and colitis.
65	Mrs. Z.	3.3	Colitis and hypertonia.
66	Mr. R.	7.0	Pulmonary tuberculosis.
72	Mrs. I.	5.2	Iritis and colitis.
73	Mr. S.	8.0	Enteritis.
74	Mr. M. N.	5.2	Duodenal ulcer.
76	Mrs. H.	6.0	Enterocolitis.
77	Mrs. H.	3.0	Iritis.
78	Mrs. H.	7.5	Duodenal ulcer.
80	G. O. M.	5.0	Otitis.
81	Mr. W.	6.0	Lead poisoning.
82	Mr. H.	5.0	Gastric ulcer.
83	Mrs. B. P.	6.2	Appendicitis and arthritis.
84	Mr. B.	5.0	Arthritis.
86	Miss S.	6.5	Amœbic colitis.
87	Mrs. M.	6.4	Amœbic colitis.
88	Mr. B.	6.0	Enterocolitis.
91	Mrs. W. S. B.	4.0	Arthritis.
95	Mrs. Ph.	7.5	Arthritis.
99	Miss C.	9.0	Appendicitis.
103	Mrs. H.	6.0	Asthma and colitis.
106	Mrs. J. S.	6.0	Enterocolitis.
107	Mrs. M.	6.0	Chronic appendicitis.
113	Mrs. B.	3.0	Appendicitis.
114	Mrs. J.	7.5	Enterocolitis.
120	R. W.	6.0	Constipation and amœbiasis.

Two cases deserve to be reported more in detail.

Case Reports.—CASE I. Mrs. M. A., gave the usual gall bladder complaint of pain and distress. Physical examination showed tenderness in both cecum and gall bladder regions. The roentgen-ray examination was negative for stone, but gave a positive path-

ological gall bladder shadow. There was a cecal stasis of more than seventy-two hours. The stool examination showed Amœba dysenteriæ. The urine was negative and the phenolsulphonephthalein elimination was 50 per cent. The first blood count showed a hemoglobin of 82 per cent; red cells, 4,290,000; white cells, 5600; neutrophils, 50 per cent; mononuclears, 43 per cent; transitionals, 7 per cent. The icterus index on June 18, 1924 was 13; on September 2, 1924, it was 10; only March 18, 1925, it was 10. A slight attack of the old trouble brought the patient to operation in April, 1924, at which time the index was 13 again. The operative findings were: A chronic cholecystitis with stone; chronic appendicitis with colon adhesions. The gall bladder was drained and the drainage was very black and profuse. At the end of the first week, the index had dropped to 8; and on leaving the hospital three weeks later, it had made a further drop to 6.4. The proven and undoubted diagnosis here was a cholecystitis, cholelithiasis, chronic appendicitis with colon stasis and adhesions; chronic amœbiasis (undoubtedly arrested) and chronic hepatitis. The clinical factor here most probably causing the hepatitis was the cholecystitis for this was the only active process, but by operative treatment the condition could be relieved. Since operation, the patient's return to normal has been excellent.

Case II.—Mr. M. came with the complaint of intermittent unconscious spells, at times accompanied by convulsions. There was marked tiredness. He had a high degree of constipation and intestinal gas. The physical examination showed a blood pressure of 100 systolic and 60 diastolic. There was a marked dermatitis herpetiformis. The heart showed a slight systolic murmur. The laboratory findings were: Hemoglobin, 90 per cent; red cells, 5,100,000; white cells, 6100; neutrophils, 58 per cent; mononuclears, 42 per cent. The urine was negative, with a phthalein elimination of 60 per cent; the icterus index was then 11.5; the Wassermann test was negative; the nonprotein nitrogen was normal; roentgen-ray showed a chronic appendicitis with cecal adhesions and a pathological gall bladder. Before operation the index was 10. Twenty-four hours postoperative, it rose to 13.5. On the afternoon of the second postoperative day he was transfused. During the night following he almost died from heart failure, but was finally stimulated through until morning. His condition was that of severe shock. At that time his index reading was 39.5. After four or five days, the index again returned to around 10 and there was no more heart disturbance. His convalescence has been slow, but steady, and his index is now down to around 7. In this case, one could almost follow his clinical history by the curve of the icterus index.

Conclusions. We believe the following conclusions are justifiable:

1. The icterus index is the test of choice for the quantitative estimation of bilirubinemia for the reason that it is simple, accurate, and of definite clinical value.

2. There is no untoward effect or danger to the patient in its use.

3. The Widal hemoclastic crisis probably tests the proteopexic function of the liver, which is allied to, but different from, the bile forming function.

4. Liver function is probably closely associated with the behavior of the blood stream leukocytes. Both of these come under the influence of any foreign protein introduced either through the intestinal tract or through the tissues elsewhere. It seems to us probable that our leukocyte tests of today may be in reality liver-function tests. Extreme leukocytosis in the presence of bile is probably the result of a high grade hemopoietic stimulant acting not because of the presence of bile, but in spite of it.

5. The icterus index is in the last analysis, a measure of bilirubin in the blood stream. Its clinical interpretation must depend on all the factors that will produce this condition. It is a valuable aid in diagnosis, prognosis and treatment. The test is neither infallible nor specific in the diagnosis of any one disease, but as other clinical tests are rated, this one has a high marking.

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MITRAL STENOSIS AFTER THE FIFTH DECADE OF LIFE.

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It is currently believed that mitral stenosis is a serious valvular lesion, which entails a grave prognosis, and predicates a lethal outcome before early middle age. Such at least is the teaching in most text books. Robinson,[1] in Nelson's system, places the average age at death as thirty-five years. Most authors refer to the studies of Samways,[2] who, on analysis of 196 necropsies of patients with mitral stenosis found the average age at death to be thirty-eight years, of Duckworth,[3] who reported this lesion as unusual after the age of forty-five and of Gillespie,[4] who, from a study of the records of the Edinburgh Hospital, placed the average age at death in the fourth decade for men and in the fifth for women.

We have been impressed at Montefiore Hospital with the frequency of mitral stenosis in patients who are over fifty years of age, and in order to obtain a more accurate idea of the incidence of this valve lesion at a relatively advanced age, we have studied the records of all patients who were discharged during the last three years with the diagnosis of mitral stenosis. Very many of these were under our personal care during their stay in the hospital.

Montefiore Hospital is a hospital for chronic diseases, that is, it admits as patients individuals of all ages whose disability is such that a prolonged period of hospitalization extending over many months is necessary. Consequently, the patients are selected to a certain extent. Patients with heart disease, for instance, are usually those endowed with a very poor cardiac reserve, as a result of long standing cardiac disability. Early cases are not seen, as a rule.

During the last two and a half years 183 patients of all ages, including children, were discharged from or died at Montefiore Hospital with the diagnosis of mitral stenosis. Of these, 46, or exactly one-quarter, were over fifty years of age. The average age of this group was 57.7 years, and the oldest patient was eighty-three years. Every one of these cases was well authenticated. A careful search of the literature reveals further evidence that mitral stenosis is not so rare at an advanced age. Thus Mackenzie, in his book on *Diseases of the Heart*, states that patients with a non-progressive mitral stenosis may reach old age without symptoms.

Gillespie[4] tabulates the age distribution of 535 cases of mitral stenosis as follows:

Ages.	Male.	Female.	Total.
1 to 9	9	4	13
10 to 19	41	72	113
20 to 29	49	95	144
30 to 39	55	57	112
40 to 49	35	28	63
50 to 69	64	24	88
69 plus	2	0	2
	255	280	535

Thus 16.8 per cent were over fifty years of age. Samways[2] found 10 per cent of 196 patients who were over sixty, and Wilson,[5] 8 per cent of 62 cases and Cabot[6] 23 per cent of 200 cases over fifty. There is enough evidence in the literature, therefore, in addition to our own findings, to indicate that mitral stenosis is not uncommon in the older age periods.

In a study such as this, one precaution in particular must be observed. In certain patients with large hearts, consequent usually on adhesive pericarditis or on hypertension, a presystolic murmur may be heard at the apex, although on autopsy no narrowing of the mitral orifice is found.[7] These cases, however, are not very common and can usually be differentiated by the absence of the characteristic small pulse of mitral stenosis, of the cyanotic mitral facies, and of the sharply accentuated pulmonic second sound.

It is a matter of considerable interest to determine the cause of the valvular disease in these older individuals, but such an attempt is fraught with many difficulties. Even in the young, cases of mitral stenosis, as well as of other valvular lesions, are seen with considerable frequency, in whom it is impossible to determine the etiologic agent. It is generally accepted that from 60 to 70 per cent of patients with chronic valvular disease give a history of some previous rheumatic infection. In the remainder the cause of the valvular lesion usually remains a matter for speculation. If such a situation obtains in the younger age groups in whom memory is not yet dimmed by the lapse of time, it is evident that in elderly persons the number who can assign a definite cause for their heart disease will be still smaller; for, with the passing years, the recollection of minor illnesses becomes increasingly hazy.

It is not astonishing, therefore, that of our 46 patients only 17, or 37 per cent, gave a clear history of a typical rheumatic infection. We have classed 3 additional cases with the definite rheumatic group because of the fact that they evidenced aortic as well as mitral lesions, and in 1 case an adhesive pericarditis, and because 2 of them on necropsy presented typical healed verrucæ. Thus 20 of the 46 cases may safely be assigned to the rheumatic category.

In the group of mitral stenosis of undetermined etiology, we have

placed 12 patients who remembered no rheumatic infections, but who corresponded in their clinical manifestations to those discussed in the previous paragraph. They were, with one exception, under sixty years of age, were well nourished, with the typical mitral stenosis facies and a tendency to a plethoric appearance. In the case of many of these, were an accurate history obtainable, one would undoubtedly find indications of mild rheumatic episodes in childhood or in early adult life.

Finally, there is a group of patients who, with one exception, were over sixty years of age, in whom, too, there was no history of antecedent infections, but who, in addition to the physical signs of mitral stenosis, gave evidence of widespread arteriosclerosis of both peripheral and central vessels. These patients, as a rule, did not present the typical full-blooded appearance of the ordinary mitral patient, but were more poorly nourished and of a more sallow complexion. In them various complications, such as cerebral hemorrhage, cerebrospinal arteriosclerosis and diabetes, occurred. We have ventured to diagnose these cases as atherosclerotic mitral stenosis. We are well aware that a number of them might with propriety be placed in the "undetermined class," but we believe that the existence of an atherosclerotic form of mitral stenosis is sufficiently well established to warrant this classification, and to justify drawing attention to its frequency.

Huchard,[8] some thirty years ago, was the first to describe this type of mitral stenosis, which he called "le rétrécissement mitral des arteriosclereux." He distinguished two forms: (1) An atherosclerosis implanted on an ordinary mitral stenosis; (2) a primary atherosclerotic mitral stenosis. He believed that in these cases the degree of narrowing of the valve was less than in the endocarditic type, and that the aperture, instead of being funnel, or buttonhole shaped, was more irregular, and in the figure of a cross or of an hour glass. In his usual didactic manner he built up a complete symptomatology about this lesion, and pointed out that the characteristic clinical picture was often masked by the associated presence of hypertension in the greater circulation. Some years earlier Pitt[9] had published a paper on the association of granular kidneys with mitral stenosis, and had shown that in many instances both lesions were found in the same individual. The average age at death of his cases was fifty-two years for men and forty-two for women. Some years ago Cowan and Fleming[10] reinvestigated this relationship between renal fibrosis and mitral disease and found a close correlation between the two. Their findings are not pertinent to the question we are discussing for they included both mitral stenosis and mitral insufficiency in one table. That atherosclerotic mitral disease associated with mitral insufficiency is common in patients with hypertension and nephrosclerosis is common knowledge. Their assumption, however, that in patients with mitral stenosis

who give no history of antecedent infectious disease, either atherosclerosis or chronic nephritis, is the cause of the heart lesion, is supported by insufficient evidence. Indeed, the relatively young ages of their patients and the well-known insidious progress of rheumatic infection speak against this view.

More recent writers have minimized the importance of atherosclerosis as a factor causing mitral stenosis.[11] Anitschkow,[12] indeed, on the basis of pathologic studies, reaches the conclusion that atherosclerosis can produce no deformity of the heart valves, but can only increase their rigidity to some extent. He believes that the fatty degeneration and calcification seen in distorted valves is a secondary change following necrosis of an old inflamed area. His reasoning does not seem quite sound, when one recalls the great ulcerations and deformities that are seen so frequently in the aorta consequent solely on atherosclerosis.

Many pathologic studies of atherosclerosis of the heart valves have been made and several types have been distinguished. The opaque yellow flecks of atheroma on the ventricular surface of the aortic leaflet of the mitral valve have been well described by Beitzke.[13] These rarely, if ever, are of sufficient extent to produce the picture of clinical valvular disease. More significant is the same disease process when it is localized at the site of insertion of the mitral valve in the fibrous auriculoventricular ring and in the ring itself. Here the sequence of deposits of fat and cholesterol crystals, followed by calcification is very common, and leads to a typical pathologic picture which Dewitzky[14] named annular sclerosis. In the advanced stages of this annular sclerosis large calcified nodules and strands are formed which may project into the lumen of the mitral orifice. At times there is secondary bone formation. The development of a complete calcified ring narrowing the mitral orifice is rare.[15] At times this process by impinging on the bundle of His may injure it and so produce heart block.

Two of our patients who came to necropsy illustrate very well the manner in which atherosclerosis may cause mitral stenosis. As is apparent in Fig. 1, the significant lesion is the complete nodular calcification of the mitral ring which definitely narrows the auriculoventricular orifice; but to a lesser degree than does the typical endocarditic form of mitral stenosis. The mitral leaflets are thickened and sclerotic but not fused. The pathologic picture is not so clear cut in most cases, for combination forms of atherosclerosis superimposed on infectious valvular disease are common, so that it may be impossible to classify the lesion from the point of view of its etiology.

Since there is this difficulty in distinguishing the nature of the valvular disease at the autopsy table, it is not astonishing that in the clinic one often is unable to decide in the individual case whether a pure atherosclerosis or an old endocarditis has determined the

FIG. 1.—Arteriosclerotic mitral stenosis: Nodular calcification of annulus fibrosus.

FIG. 2.—Roentgen-ray picture of auriculoventricular ring of Fig. 1.

lesion. The following diagnostic features, which, however, cannot be considered absolute, are characteristic of atherosclerotic mitral stenosis: (1) The absence of a history of rheumatic infection, or of another infection that might be considered as the pathogenic agent; (2) evidences of advanced arteriosclerosis in the peripheral or visceral arteries; (3) generally a poor nutrition and a sallow nonplethoric appearance; (4) complications ordinarily associated with arteriosclerosis; (5) an advanced age—usually beyond sixty.

The mistakes that may enter in such a diagnosis are manifold. As is apparent from the table, a negative history is no proof that no rheumatic infection has been experienced. Two of our patients classed as arteriosclerotic had had bronchiectasis for many years, 1 for ten and 1 for twenty-two years. It is impossible to determine whether or not this served as a source of infection of the valve. The presence of arteriosclerosis in one region of the body can be taken in only the most general way as evidence of a similar change in other vascular structures. Moreover, it is always possible that atherosclerosis may develop independently in a person with an endocarditic mitral stenosis. The age of the patient is a more or less arbitrary criterion which may result in placing survivors of the rheumatic group in the atherosclerotic category. The preponderance of females over males among our patients in the proportion of almost 2 to 1 corresponds to the sex distribution in the younger age groups. Were atherosclerosis a very frequent factor, one would expect men to exceed the women in numbers.

Of 147 patients of all ages with mitral stenosis, the auricles were fibrillating in 75, or over 50 per cent. In the series of patients over fifty years of age, 26 or 56.5 per cent were accompanied by auricular fibrillation. However, only 36 per cent of the atherosclerotic group, in contrast to 70 per cent of the rheumatic group, had this complication. The incidence of an elevated blood pressure is difficult to evaluate because of the limited number of cases. Hypertension, however, seems more common in the atherosclerotic form of the disease.

The study of this group of elderly patients with mitral stenosis reveals a number of other interesting facts. The 30 women had given birth to 119 children, or an average of almost 4 children to a woman. Only 6 of the women had no children, while 2 had 10 and 1 had 12 offspring. From the histories one cannot determine the age at which the heart lesion actually developed, for these patients characteristically manifested no symptoms until they were well past middle age. Many of the rheumatic group, however, told of attacks of arthritis in childhood or in early adult life, so that it seems probable that in many instances the mitral stenosis was well established during the childbearing period, and that the women underwent repeated pregnancies without cardiac distress.

TABLE I.—MITRAL STENOSIS IN PATIENTS OVER FIFTY.

Case number.	Sex.	Age.	Number of children.	Auricular fibrillation.	Blood pressure.	History.	Duration of cardiac symptoms in years.	Notes.
				RHEUMATIC MITRAL STENOSIS.				
8,129	F	55	0	−	110/60	Arthritis at 18	20	Died; aortic stenosis and regurgitation
8,242	F	57	1	+	150/88	Arthritis in childhood	2	Died
8,822	F	56	6	+	214/114	Arthritis, tonsillitis	14	Died; necropsy; tricuspid stenosis; granular kidneys
9,709	F	51	3	−		Subacute arthritis on admission	10	
9,780	F	52	3	+	90/60	Arthritis at 50.	2	
10,069	F	54	3	−	130/60	Arthritis from 24 to 34	3	Aortic insufficiency, diabetes
10,110	F	50	5	+		Arthritis at 31 and 37	1	
10,294	F	52	0	+	130/70	Arthritis from childhood to 46	2	Aortic stenosis and insufficiency
10,545	F	55	12	+	145/60	Arthritis at 48; tonsillitis at 22	7	
11,695	F	55	3	+	130/90	Arthritis at 47	7	Aortic stenosis and insufficiency; bronchiectasis
10,683	F	53	7	+	230/120	Many sore throats; "rheumatism" at 37	10	Moderate sclerosis of radials
11,245	F	55	5	−	180/100	Sore throat, rheumatism, chorea at 15	½	Spondylitis; diabetes
8,482	M	56		+	140/80	Arthritis at 44	11	Died; necropsy: general ararteriosclerosis; cardiac thrombosis
8,000R	M	56		−	110/60	Negative	25?	Died; necropsy; adherent pericardium, aortic insufficiency, verrucous endocarditis
9,557R	M	52		+	144/90	Rheumatism at 12	7	Embolism left brachial artery
9,449	M	54		+	120/70	Negative	4	Died; aortic and tricuspid insufficiency
9,755								

9,557R	M	52		+	144/90	Rheumatism at 12	7	Embolism left brachial artery
9,449	M	54		+	120/70	Negative	4	Died; aortic and tricuspid insufficiency
9,755	M	51		+	110/70	Arthritis at 41 and 49	1	
10,636	M	56		+	110/50		2	Died; necropsy; healed verrucæ on mitral and pulmonary valves
11,118	M	52		+	122/85	Arthritis at 25	5	
9,279	M	64		−	110/60	Polyarthritis at 7	½	Died; necropsy; mitral ring calcified; radials and coronaries sclerosed; Streptococcus viridans infection of valves
MITRAL STENOSIS OF UNDETERMINED ORIGIN.								
8,105	F	52	6	+	130/70	Negative	15	Hemiplegia
8,909	F	50	6	+		Negative	2	Adenoma of thyroid
9,236R	F	55	0	−		Tonsillitis	?	Died; aortic insufficiency; carcinoma of cervix
9,621R	F	56	10	−	145/90	Negative	5	Endometritis after second childbirth
9,926	F	54	7	−	160/85	Empyema at 40	8	
10,102	F	56	?	−	176/90	Chills and fever at 44	15	Aortic insufficiency
10,267	F	64	1	+	146/80	Negative	1	Died
10,433	F	53	5	+	186/98	Negative	1	Hemiplegia
10,469	F	58	0	+	138/76	Negative	1	
8,888	M	53			140/76	Negative	1	Arteriosclerosis; radials and temporals
10,247	M	59		+	118/70	Negative	1½	Gastric ulcer
11,363	M	53		−	208/70	Negative	1	Hemiplegia; aortic insufficiency; sclerosis of radials
ARTERIOSCLEROTIC MITRAL STENOSIS.								
9,330	F	83	4	−	210/130	Negative	1	Died; necropsy; mitral ring calcified, leaflets thick and sclerotic, chordæ shortened; cerebrospinal arteriosclerosis

TABLE I.—MITRAL STENOSIS IN PATIENTS OVER FIFTY.—(*Continued.*)

Case number.	Sex.	Age.	Number of children.	Auricular fibrillation.	Blood pressure.	History.	Duration of cardiac symptoms in years.	Notes.
			ARTERIOSCLEROTIC MITRAL STENOSIS.—(*Continued.*)					
10,527	F	60	0	+	145/60	Negative	4	Died; diabetes; arteries thick and tortuous
11,063	F	65	7	−	135/80	Bronchiectasis, 10 years	1	Bronchiectasis
11,125	F	66	2	−	130/75	Negative	1	Died; great emaciation; radial sclerosis
11,205	F	61	7	−	110/76	Pneumonia at 38; bronchiectasis	0	Examined twelve years ago; heart normal; eleven years ago systolic murmur with cardiac enlargement
10,332	F	68	5	−	180/110	Negative	0	Hemiplegia; arteriosclerosis
10,537	F	62	3	+		Negative	½	Poor nutrition; radials sclerosed
9,049	F	54	1	+	155/70	Negative	4	Obese; angina pectoris
12,024	F	60	7	−	120/64	Negative	½	Died; radials thick and tortuous; several apoplectic strokes
8,855	M	68		−	160/70	Negative	2	Arteries sclerotic; bundle branch block
10,642	M	61		+	150/60	Negative	6	Four years ago had simple mitral insufficiency; sclerosis of radials
10,772	M	62		+	184/100	Negative	5	Hypertension five years; general arteriosclerosis
11,119	M	69		−	138/90	Negative	0	Died; carcinoma of stomach; marked arteriosclerosis
11.136	M	68		−	100/66	Negative	10	Died; necropsy; mitral ring calcified; leaflets thick and calcified

As is apparent from Table I, in most instances many years elapsed between the attack of arthritis and the present symptoms of heart disease. The most striking case is that of a man sixty-four years of age, who had had an attack of polyarthritis when he was seven years old, and none subsequently.

TABLE II.

	Rheumatic.	Undetermined.	Arteriosclerotic.	Total.
Number of cases	20	12	14	46
Age range in years	50 to 64	50 to 64	54 to 83	
Average age in years	54.4	55.1	64.8	57.7
Sex:				
Male	8	3	5	16
Female	12	9	9	30
Auricular fibrillation:				
Number	14	7	5	26
Per cent	70	58	36	56.5
Diastolic blood pressure over 90	3	1	3	7
Systolic blood pressure over 140	6	6	7	21

Summary. Mitral stenosis is not uncommon in the sixth and seventh decades of life. In most instances it is the end result of a rheumatic infection in childhood or early adult life. The mitral narrowing is not extreme, and the lesion is nonprogressive, or very slowly progressive, so that significant symptoms do not develop for many years. Women with such a condition may apparently undergo many pregnancies without distress and without injury to the heart.

In a certain number of cases of mitral stenosis in elderly persons, the valvular lesion cannot be interpreted as the end result of a ancient endocarditis, but must be regarded as a primary atherosclerosis of the mitral valve, and particularly of the auriculoventricular ring. The characteristic pathologic finding is a widespread calcification of the mitral ring encroaching on the lumen of the auriculoventricular opening with thickening and at times calcification and fusion of the valve cusps.

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ATYPICAL TABES DORSALIS (FORME FRUSTE): SURGICAL ERRORS IN, WITH LEADING POINTS IN DIAGNOSIS.*

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The purpose of this paper is to point out some mistakes that are made in the diagnosis of the incomplete or atypical form of tabes dorsalis. These mistakes at times lead to needless surgical operations. It is also my purpose to illustrate with a case report, facts long recognized in neurological circles, but at times overlooked in general medical and surgical fields.

It is now over fifty years since Charcot first linked up gastric crises with tabes dorsalis as a cause of acute abdominal distress and emphasized the fact that preataxic crises may occur years before locomotor trouble. He also described the "forme fruste" or atypical type with this condition. Even with improved methods of study and diagnosis of our cases, we still see far too numerous mistakes. Some of the reasons for these errors are: (1) That the cases usually having crises are not typical. Many cases, probably one-half, deviate from the text-book picture of tabes dorsalis, which any layman can recognize in the end-stages as locomotor ataxia. The cases differ either by the presence of rare symptoms or the symbiosis of other associated diseases. (2) We fail to make a correct interprepetation of the case because too often the disease is not looked for. Hurried histories, incomplete examinations particularly neglecting the nervous system and a failure to remember that the root pains of cerebrospinal syphilis may simulate almost any abdominal lesion, account for many errors. (3) In doubtful cases spinal fluid examinations are not resorted to frequently enough. A few physi-

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cians are still under the impression that a negative blood Wassermann test rules out neurosyphilis, of course we now know this is not true. In some of these doubtful cases an exploratory laparotomy has been done where a spinal puncture might have settled the diagnosis. In a small percentage of cases the spinal fluid examination will not clinch the diagnosis as illustrated in my case, but in the large majority of instances this examination would settle the question.

The following case report presents many interesting facts in the ten-year course of the disease. Records were obtained from the various hospitals in which the patient received five major abdominal operations.

Case Report. Mr. J. T., aged forty-four years, first came under my observation at the Philadelphia General Hospital, April 5, 1923. He complained of attacks of pain in the abdomen, with vomiting. At nineteen years of age he contracted a chancre and received six weeks of treatment. He had no secondary eruption. In 1912 he began having attacks of sharp cutting shooting pains in the back, abdomen and legs accompanied by vomiting. These attacks at times lasted two weeks, recurring at intervals of four to five weeks. In July, 1913, he was admitted to a well-known Philadelphia hospital for an exploratory laparotomy. The surgeon found the stomach normal; no masses, pylorus normal, the liver smaller than normal with many small nodules, "hob nailed," and gall bladder normal. The appendix was retrocecal but apparently normal. The diagnosis was cirrhosis of the liver. He was discharged in six weeks only to return one week later with an attack of pain and vomiting. Another surgeon advised operation and this time a posterior gastroenterostomy was done. The liver was found cirrhotic and there were a few adhesions about the pylorus. The abdominal organs were otherwise normal. He continued to have the same attacks at irregular intervals, returning to this hospital off and on until August, 1921, when a third operation was performed, which was advised against by the surgeon but insisted upon by the patient. This incision was over the gall bladder. Multiple adhesions were found and the abdomen was closed without interference. It should be stated now that in addition to his attacks of pain and vomiting since 1918 he had urgency, precipitancy and dribbling of urination. Since 1920 he had lost his sexual power. Following his third operation the attacks persisted and in June, 1922, he was admitted to another hospital on the service of a well-known surgeon.

Here another exploratory operation was performed; innumerable adhesions were found and after working for two hours the surgeon abandoned the operation. In two weeks the same old attacks returned and were only relieved by morphin.

In September, 1922, he was readmitted, on another well-known

surgeon's service, because of persistent vomiting. At this time a very complete study was made from a general physical and laboratory standpoint, but no mention was made of the nervous system. His general physical status was essentially negative as were all laboratory tests including a blood Wassermann. The gastro-intestinal study revealed a marked stasis in the ileum and a gastro-jejunal ulcer was considered. The surgeon who later reported the case states in his report: "The patient begged me every day to operate on him, I kept him in the ward long enough before the operation to be sure that he really was suffering and not merely neurasthenic." He felt the trouble was due to a vicious circle in his former gastroenterostomy. At the fifth operation he also found adhesions everywhere and with difficulty dissected the jejunum from adhesions, found no ulcer, but the duodenal loop was obstructed so the old anastomosis between the jejunum and stomach was separated. Four days after this operation the patient again vomited. More roentgen-ray studies were made, all efforts were focused on finding a cause within the abdomen; the possibility of root pains seems not to have been considered. The surgeon's further report is interesting because of his interpretation of the case: "The only criticism that I think I could make in addition to condemning the unnecessary operations which have been done upon him is that he has never had his appendix removed and perhaps I should have done it myself, but he had enough trouble when he was under my care to make me willing to postpone that for another occasion."

The patient continued to have his attacks before and after admission to the Philadelphia General Hospital. A complete neurological study revealed the following facts: Inequality of the pupils with the right pupil reacting slower to light than accommodation, diminished pain sense over the left lower thoracic region and over the left leg below the knee. The knee jerks were both active; the right Achilles was absent and the left was subnormal with hypotonia of the leg muscles; there was no ataxia. A cystoscopic examination revealed a relaxed vesical sphincter; the musculature looked like that seen in tabetic bladders, and the posterior urethra was anesthetic. The urologist stated the urinary frequency and urgency was entirely due to failure of proper innervation of the bladder musculature. Complete laboratory studies, including gastric analysis, blood chemistry and gastro-intestinal roentgen-ray were essentially negative. Two blood and spinal fluid Wassermann tests were negative. A diagnosis of atypical tabes with involvement of the thoracic and sacral segments was made, but not sufficient lumbar involvement to catch the patellar reflexes. He was given 16 neoarsphenamin injections and discharged in July, 1923.

The patient again came under my observation in September, 1923, at the Philadelphia Orthopedic Hospital and Infirmary for Nervous Diseases on the service of Dr. F. Sinkler. He gave the

same old complaint. Serological studies of the blood and spinal fluid were again entirely negative. The neurological status was the same as before except that he now showed a right-sided Babinski reflex. After several severe attacks of pain and vomiting he was given 4 Swift-Ellis intraspinal injections, after these he showed a bilateral Babinski. The blood Wassermann as always negative but a provocative reaction from the intraspinal injections produced a strongly positive spinal fluid Wassermann for the first time and gave a gold curve of 4554321000. The fluid a short time later became negative. He continued to have attacks of pain in the abdomen and legs usually accompanied by vomiting. Several times he had peculiar attacks of sudden unconsciousness in which he became pulseless and respirations ceased for about thirty seconds.[1] There was no convulsion and consciousness was regained in a few minutes. The patient had complete amnesia for the attacks. In view of his continued suffering without relief on vigorous treatment he was referred to Dr. F. C. Grant for section of his antero-lateral columns. On March 12, 1924, a bilateral chordotomy at the fifth thoracic segment was done. Following this his attacks ceased until September, 1924. He dragged his right foot some and showed pain and temperature disturbance as high as the third lumbar segment but no Babinski reflex was present. His pain reappeared in a single point 2 inches to the left of the umbilicus accompanied with vomiting. Trophic lesions developed in the form of punched out crateriform ulcers about the size of a quarter over the anterior surface of the thighs and shins. Intragluteal injections of mercury were given. Decubital ulcers formed at the site of the injections. In addition he developed an ulcerative cystitis and died November 30, 1924.

A necropsy limited to the brain and spinal cord revealed the following findings: The cerebral hemispheres showed a definite edema with flattening of the convolutions. The pia arachnoid was definitely milky and slightly thickened. The dura mater was slightly thickened. The spinal cord showed a distortion at the level of the operation and a definite thickening of the meninges to $\frac{1}{4}$ cm. was present over the posterior surface in the lower sections. Microscopic sections of the cord revealed much new connective tissue formation in the lateral parts of the cord at the site of operation. Complete degeneration was present in the cerebellar tracts. The posterior columns were only slightly affected. In one section a unilateral change was present in the column of Burdach. The anterior horn cells showed definite atrophy and degeneration.

Comment. The case requires but little comment since the story is clear and the findings positive. It should be said that no mention was made in the other hospital reports of a chancre history and it is possible the patient concealed this fact. It is indeed surprising that five different surgeons failed to consider a neurological disorder, when

after each operation he had not obtained relief from pain. The patient at various times begged for operations as they often do in the hope of relief, but this should not be sufficient excuse for surgery. From a neurological point of view the atypical findings of the disease are instructive. In twelve years there were no locomotor signs, only suggestive pupils, hypalgesia over the lower thoracic region and left leg, and one absent Achilles jerk. The serological studies which were repeatedly negative and only positive from provocative reaction illustrate the fact that a negative spinal fluid Wassermann does not rule out cerebrospinal infection in old or treated cases. The relief from pain obtained by section of the antero-lateral columns was instructive and should have been done years before instead of the other operative procedures. This operation is indicated in chronic cases where no relief is obtained from treatment and the suffering incapacitates the individual.

The incidence of gastric crises is given as occurring in 10 per cent of tabetics by Starr,[2] Holmes,[3] Hall,[4] and Leimbach.[5] Lucke[6] found 12 per cent of 250 cases had visceral crises. Bonar[7] found 16.78 per cent of 286 cases had gastric crises, while Nuzum[8] found in 1000 tabetics, crises occurring in 22 per cent. It is impossible to estimate from the sparse literature the frequency of operative mistakes in these cases. There are numerous scattered reports of isolated cases where from one to three operations were performed with no relief of symptoms; only to have the syphilitic etiology later proved and the patient's symptoms relieved by treatment. All the reported cases are by internists or neurologists and none are to be found in the surgical literature. Here one only finds occasional casual reference to the frequency of such mistakes. There are a few collections of cases from various clinics that give us some idea of the frequency of mistakes in surgical diagnosis in these cases.

Nuzum[8] reviewed the records of 1000 tabetics from the neurological service of Cook County Hospital and found 97 needless laparotomies had been performed on 87 of these patients. Of these, diagnoses of gastric ulcer and gall-bladder disease were the most frequent, with the diagnosis of appendicitis a close third. Operations had also been performed for almost every other type of abdominal lesions. Several patients had been operated upon several times. After the first incision, postoperative adhesions seem to be a favorite excuse for having a second, third, fourth or even fifth "look in."

Woltman[9] found from 120 patients having syphilitic gastric crises that 25.8 per cent had been subjected to unfruitful surgical interference and 61 operations had been performed in this group. The appendix was the most frequent supposed offender in his series, with the gall bladder second and the stomach third. The pelvic organs, kidney, colon, postoperative adhesions and in some cases exploratory laparotomy were given as diagnoses. It is surprising the number of instances in which repeated operations have been performed, on

the same patient, even after no pathological lesions were found in previous explorations, and the history obtained showed that no relief was experienced from previous operations. No suspicion that a neurological disorder might account for the symptoms ever seemed to have arisen, even after four or five surgical failures.

It is also interesting to find in these cases as well as in other reflex or functional nervous disorders how often postoperative adhesions are blamed when a correct diagnosis has not been made. Ziegler,[10] in a study of 164 psychoneurotics, found 18.3 per cent had received one or more major abdominal operations for the relief of psychoneurotic symptoms, all without avail. No report was found of a tabetic having had more than five abdominal operations. Holmes reports a case that had five abdominal operations performed before a correct diagnosis of tabes was made. One patient in Nuzum's series had been subjected to five laparotomies with no relief of symptoms. The last three were made for postoperative adhesions. Woltman, Newburgh[11] and Tuohy[12] report cases upon whom four major abdominal operations had been performed before complete neurological and serological studies proved the correct etiology to be syphilitic radiculitis. In my case the five operative descriptions have been given.

Difficulties in diagnosis are not so marked in the well advanced ataxic patient, where we find the absent deep reflexes, Argyll-Robertson pupil, positive Romberg and other classical symptoms. The fact that the so-called typical pictures are the exception rather than the rule cause our difficulties. There is no one symptom that may not be absent. For example, we hear it said, tabes was ruled out because the knee jerks were present. The knee jerks may be normal; exaggerated in both; normal in one and diminished in the other or both absent. The reflex changes depend upon the location of the pathological process; so, for instance, unless the lesion extends to the fourth lumbar segment of the cord the knee jerk will be present. If the first sacral segment is not involved the Achilles jerk will be present. Also if there happens to be accompanying lateral column disease the reflexes may be exaggerated. The preataxic stages before extensive degeneration of the posterior columns occurs is the time in which most crises occur. This was true in my case, in which there was but slight posterior column degeneration. Crises may last for years (eighteen years according to Oppenheim[13]) without marked reflex alteration. As a matter of fact the knee jerks are not absent in over 75 per cent of early cases. Hall, for example, in 100 cases found them absent in but 65 per cent; present in 22 per cent; exaggerated in 4 per cent and unequal or sluggish in 6 per cent. Frey[14] found them absent in 56.47 per cent of 850 cases. Collins[15] reports 77 per cent of 140 cases had absent knee jerks in the preataxic stages and 84.3 per cent in the well advanced stages. Statistics from various clinics of large groups of

cases in the later stages show higher percentages with absent patellar reflexes. Thomas[16] in 111 cases reports absent knee jerks in 81 per cent, Mendel and Tobias[17] found them absent in 82 per cent, Lucke in 90 per cent, Leimbach in 92 per cent and Bonar reports 95 per cent of 286 cases had absent patellar jerks. Riley[18] states 90 per cent of 61 cases had absent knee jerks. He also in another report[19] gave 7 cases of tabes with knee jerks retained or exaggerated.

The same thing is true for the Argyll-Robertson pupil and Romberg's sign. These classical signs are present in only a little over one-half of the early cases. In such a disease with variable symptoms and signs we must take the picture as a whole to establish a diagnosis. The following combination of symptoms and signs in order of frequency would catch most cases. The history of onset with the development of the subjective sensations is important. The story of the lacinating pains as though shot, occurring irregularly, of momentary duration leaving behind an intensely sore spot is another. These pains may be the only complaint for several years with no objective neurological findings present except a positive spinal fluid. The paresthesias—a sense of numbness in the feet with a feeling as though walking on air or associated with an uncertainty in placing the feet without looking—or a girdle sensation about the abdomen, are usually early symptoms. Pupillary changes such as inequality, irregularity, with often a loss of the consensual reflex are present before the Argyll-Robertson pupil appears. The common chest-zone anesthesia, with loss of pain sense more marked than that of touch, also hypalgesic areas over the face, thorax or extremities, are early findings. These patients early cannot recognize the vibration of a tuning-fork over the malleoli, patella or sacrum, or tell in what position the toes are placed. The loss of the normal muscle, testis, ulnar or Achilles tenderness from pinching is often striking. The Achilles jerks are often diminished, unequal or absent before the patellars. Many patients early in the disease complain of urgency, precipitancy or incontinence of urination and beginning impotence. Isolated cranial nerve palsies, eye symptoms (diplopia, ptosis) or primary optic atrophy may be early signs in certain cases. When the disease is well advanced there will usually be ataxia, Romberg's sign, and unequal, sluggish or absent knee jerks. These lattter findings when present are of extreme value but their absence does not necessarily rule out tabes. To establish an absolute diagnosis in all cases of doubt, spinal serological studies should be done. An increased total protein content, pleocytosis and a positive Wassermann are generally present, remembering that in late tabes only 75 per cent are positive. A provocative reaction in negative cases will bring out more positives.

There are many facts lost through faulty technic in a neurological examination, especially the early changes. In studying pupils it is important to study contour, size and equality as well as taking

the consensual light reflex, because often there is a loss of response when the light is thrown on the opposite retina before the typical Argyll-Robertson phenomenon appears. Another important point in pupillary examination is to avoid the accommodation reflex in testing for light reaction, by having the patient focus on a distant object, then play the beam of light in from the side of the eye. The tuning-fork test and Achilles jerks are too frequently neglected. To obtain the Achilles jerks it is important to have the patient in a comfortable kneeling position with the gastrocnemius muscles relaxed.

Gastric crises may simulate any gastro-intestinal condition and may appear early in cerebrospinal syphilis, even being the sole complaint before any of the older signs of the disease are present. Even then they are fairly unique in their manifestations. They may be present either as pain or vomiting alone, or both together, which is more common. The onset is usually sudden with mid-line pain, without reference to meals or the character of food. The pains are dull or sharp, often shooting and of agonizing character associated with sialorrhea, extreme nausea and vomiting, and great prostration and lasting a few hours to several days. Then the pains cease abruptly, with surprisingly rapid recovery of the patient, only to recur again in a few days, weeks or months. During the attacks, while the abdomen may be hypersensitive to light touch, there is no deep tenderness to palpation and there is no muscular rigidity. The attacks are almost always afebrile; in rare instances there may be pyrexia but without leukocytosis. Often relief is obtained by a hypodermic of adrenalin and in gastric crises after adrenalin the blood pressure usually falls instead of being increased as in the normal reaction. In a differential diagnosis it should be remembered that crises are not always typical and do not always commence and end suddenly but may be present as vague gastric distress. The attacks with severe retching and vomiting without pain are particularly hard to determine. Intestinal, rectal and bladder crises also occur. It should not be forgotten that hematemesis may occur in crises, but of course this should excite suspicion of an organic lesion. Then the possibility of a coëxistent gastro-intestinal lesion with tabes such as gastric ulcer[20] should be kept in mind. The possibility of the unusual condition of syphilis of the stomach must also be considered.

This report is not given in the spirit of criticizing the surgeon who is unfortunate enough to operate upon such patients. He cannot be expected to be a neurologist and often these atypical cases are extremely difficult of diagnosis. For the patient's welfare and the surgeon's happiness he should study his patients carefully, especially those with recurrent abdominal attacks presenting scars from previous operations and these who give a history of "no relief" following previous operations or "nothing wrong was found." Whenever

in doubt it is far safer to have a complete neurological study and a spinal fluid examination made and more satisfactory in the end than having opened an abdomen by mistake.

Summary. Atypical or "forme fruste" type of tabes is the most frequently missed form of the disease. Gastric crises in this variety often lead to unnecessary abdominal operations.

Incomplete histories, careless examinations and infrequent spinal punctures in doubtful cases account for most errors. Gastric crises occur in from 10 to 20 per cent of all cases of tabes dorsalis.

Reliable reports indicate that more than 10 per cent of tabetics have needless operations performed at least once upon a mistaken diagnosis. There are frequent reports in the literature of patients having had four or five abdominal operations when the cause of the symptoms was root pains of syphilis.

The classical signs of tabes are absent in approximately one-half of the early cases, when abdominal pains may be present. The knee jerks are normal or exaggerated in at least 25 per cent of early cases. The same applies to ataxia, Argyll-Robertson phenomenon and other later signs. Approximately 10 per cent of cases remain atypical throughout the entire course of the disease.

A complete life story of the individual with a careful analysis of the onset and development, a careful neurological examination and a spinal fluid study should be made where there is the slightest doubt as to a diagnosis.

In patients presenting recurrent abdominal attacks with no relief from previous operations, the possibility of an atypical form of tabes dorsalis should be very firmly impressed upon the minds of surgeons, in order to decrease the all too frequent incidence of unnecessary operations upon tabetics.

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GLUCOSE TOLERANCE TESTS IN CHILDREN.

I. Based on Body Weight.
II. Based on Nutritional Surface and Body Surface.

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I. Based on Body Weight. The sugar tolerance of children between the ages of three and twelve years has not been as carefully studied as the tolerance of adults or infants. This work was undertaken with the expectation of establishing a standard test for normal children.

The children tested were in the children's surgical wards of Mt. Sinai Hospital. The majority were Jewish children of Russian parentage. These children were, as far as could be ascertained, in good health and had been admitted to the hospital for some surgical procedure such as inguinal hernia, internal strabismus, or some minor nose and throat operation. These children presumably had had no acute infection for several weeks before admission. These tests were done before the surgical procedure; if this was not possible, several weeks were permitted to elapse after operation. Eighty-four children in all were tested, 14 of whom were retested, making 98 tests in all. Seventy per cent of the children tested were males. This predominance of males was merely accidental.

The test was begun after an overnight fast of fourteen hours.

The children were kept in bed until the test was completed. Epstein's modification of the Benedict microchemical method for blood sugar was used, the 0.2 cc. of the blood being obtained by pricking the finger. Samples of blood were taken previous to the ingestion of the glucose, and thereafter every half hour for two hours, and a final sample three hours after ingestion of glucose, making 6 tests in all. No other food or water was permitted until the completion of the test. Picric acid was added at the time the sample was taken and the specimen kept in the ice box until analysed the same afternoon by one of us. Urine specimens were collected when possible at half-hour intervals for four hours.

Glucose was given in varying amounts ranging from 0.8 gm. to 3 gm. per kilo of body weight. The glucose was given in a 30 per cent solution to which a little lemon juice was added to make it more palatable. According to John,[1] this concentration of glucose has no special effect on the secretion of gastric juice or on the concentration of the blood. The glucose was weighed out the day before, the water being added just before ingestion. Pure anhydrous glucose was used, except in a few cases where granulated glucose was substituted. The latter was always analysed and due allowance made for impurities. It has been shown by Wang and Felsher[2] that the absorption curve of the pure and the granulated glucose is essentially the same.

In order to determine the tolerance of these children for varying amounts of glucose, regardless of age, they were divided into 3 groups as seen in Table I. The amount of glucose given to the children of Group II is comparable to that generally given to adults. Janney[3] believed that 1.8 of glucose per kilo of body weight was the correct amount. Others advocate giving 100 gm. of glucose to all adults regardless of body weight. This would mean about 1.5 gm. of glucose per kilo of body weight in a normal individual weighing 68 kilos or 150 pounds.

TABLE I.—TOLERANCE BASED ON VARYING AMOUNTS OF GLUCOSE PER KILO BODY WEIGHT.

Group.	Glucose per kilo, gm.	End of 2 hours.			End of 3 hours.		
		Total cases.	Returned to fasting level.		Total cases.	Returned to fasting level.	
			Cases.	Per cent.		Cases.	Per cent.
Group I . . .	0.8 to 1.6	33	15	45	32	25	78
Group II . . .	1.7 to 1.9	19	5	31	19	17	89
Group III . . .	2.0 to 3.3	46	11	24	39	25	64

The tolerance of each group is recorded in Table I. The number and the percentage of cases in which the blood sugar returned to the fasting level at the end of two hours and at the end of three hours is recorded.* In Group I, 45 per cent of the cases returned to the fasting level within two hours. An additional 34 per cent returned to the fasting level within three hours, making a total of 79 per cent of this group returning to the fasting level within three hours. In Group II of this table it is shown that 31 per cent returned to the fasting level within two hours and an additional 58 per cent within three hours, a total of 89 per cent. In the third group 24 per cent reached the fasting level in two hours, and 40 per cent more in three hours, making a total of 64 per cent.

It appears, therefore, from these cases that in only about 83 per cent of normal children receiving less than 2 gm. of glucose per kilo of body weight, will the blood sugar return to the fasting level at the end of three hours. It is difficult to understand why the blood sugar of so large a percentage of children (17 per cent) does not return to the fasting level at the end of three hours. This delay may be due to the rate of absorption from the intestines, some individuals absorbing more slowly and therefore maintaining their blood sugar at a higher level for a longer period. John[1] believes, however, that this delay in absorption is of no great importance. On the other hand the power to convert and store excess glucose, in the form of glycogen, by the liver or the extraction of glucose from the blood by the tissues may not be so well developed in some children as others. This possible irregularity in absorption and storage may also account for the fact that the blood sugar in 60 to 80 per cent of adults[4] returns to the fasting level in two hours, whereas it takes three hours in children. The factor which controls the removal of sugar from the blood stream has yet to be determined.

Previous workers have stated that the younger the child the better the glucose tolerance. This fact has been substantiated by our findings. The children were divided into 3 groups according to their ages as seen in Table II. Each group was then subdivided according to the amount of sugar given, namely, those children receiving less than 2 gm. per kilo of body weight and those receiving more than 2 gm. per kilo of body weight.

Table II shows that children of all ages receiving less than 2 gm. per kilo of body weight have about the same tolerance at the end of three hours: 73 per cent in the younger children and 77 per cent in the older children. However, when over 2 gm. of glucose per kilo of body weight were given, the younger child had an excellent tolerance, 96 per cent returning to the normal in three hours, whereas in the older group only 43 per cent returned to the normal.

* For practical purposes those cases whose blood sugar returned within 15 mgm. of the fasting level, were included in the total percentage.

TABLE II.—GLUCOSE TOLERANCE IN RELATION TO AGE AND AMOUNT OF GLUCOSE PER KILO BODY WEIGHT.

Age, years.	Glucose per kilo, gm.	End of 2 hours.			End of 3 hours.		
		Total cases.	Returned to fasting level.		Total cases.	Returned to fasting level.	
			Cases.	Per cent.		Cases.	Per cent.
3 to 6	1.5 to 1.9	16	7	44	16	12	73
	2.0 to 2.9	26	7	27	24	23	96
7 to 9	1.2 to 1.9	13	2	16	13	10	77
	2.0 to 3.3	10	0	0	7	2	28
10 to 13	0.8 to 1.9	23	10	43	23	18	78
	2.0 to 3.0	10	3	30	7	4	57

Special comment must be made of those children from seven to ten years of age receiving over 2 gm. of glucose per kilo of body weight. In 7 cases tested only 2 returned to the fasting level in three hours. None returned to the fasting level in two hours. The number of cases is too small from which to draw any conclusions. It would be of interest to study a large group between these ages in order to ascertain if there really is a decreased tolerance at this period of childhood.

TABLE III.—GLUCOSE TOLERANCE PER KILO BODY WEIGHT IN RELATION TO AGE, AMOUNT OF GLUCOSE, AND STATE OF NUTRITION.

Age, years.	Glucose per kilo, gm.	Variations from Baldwin-Wood standard, per cent.	End of 2 hours.			End of 3 hours.		
			Total cases.	Returned to fasting level.		Total cases.	Returned to fasting level.	
				Cases.	Per cent.		Cases.	Per cent.
3 to 6	<2	−7	2	2	100	2	2	100
		Normal	11	5	45	11	8	73
		+10	3	0	0	3	2	66
	>2	−7	5	1	20	4	3	75
		Normal	17	7	41	16	15	94
		+10	3	0	0	3	3	100
7 to 13	<2	−7	9	2	22	9	9	100
		Normal	18	6	33	17	14	82
		+10	12	4	33	11	5	45
	>2	−7	9	0	0	6	2	33
		Normal	8	2	25	7	3	42
		+10	1	0	0	0	0	0

To determine whether the carbohydrate tolerance is affected by the state of nutrition the children were grouped into 3 classes in accordance with the Baldwin-Wood Height, Weight, Age Tables as seen in Table III. Of the children from three to six years of age receiving less than 2 gm. of glucose per kilo of body weight, those classified as underweight seem to have a better tolerance than those classified as normal or overweight. When given more than 2 gm. of glucose, however, the tolerance seems to be the same regardless of the state of nutrition. The number of cases is yet too small to draw any definite conclusions. At the end of two hours many of the underweight and normal group had reached the fasting blood sugar level, but in none of the overweight children did this occur.

The tolerance for less than 2 gm. of glucose per kilo of body weight is good in children over six years of age whose state of nutrition is poor or normal. The tolerance for over 2 gm. of glucose per kilo of body weight of all older children is poor. No comparative study can be made in this group.

It is our impression, however, that the overweight children should not receive the same amount of glucose per kilo of body weight as the normal or underweight children. Apparently in the overweight child the glucose is not metabolized or withdrawn from the blood stream by the liver and other tissues as rapidly as in the normal or underweight child. There must be a difference in the general metabolism of such overweight children, as they often gain on a diet containing fewer calories than calculated from their basal metabolism.

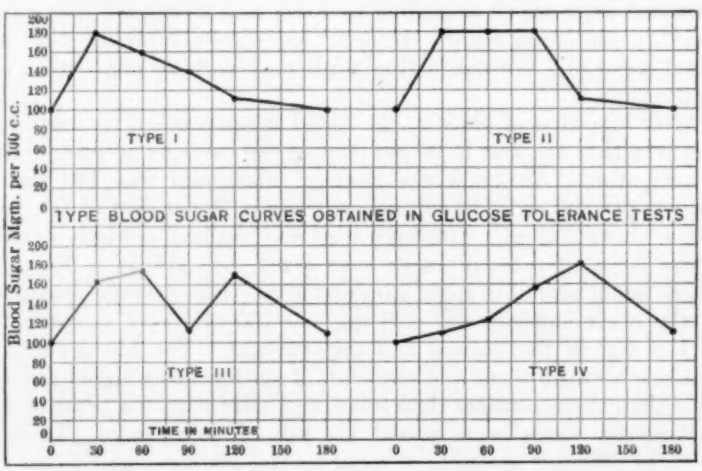
TYPE BLOOD SUGAR CURVES OBTAINED IN GLUCOSE TOLERANCE TESTS
Blood Sugar Mgm. per 100 c.c.
TYPE I
TYPE II
TYPE III
TYPE IV
TIME IN MINUTES
0 30 60 90 120 150 180

CHART I.

Four distinct blood-sugar curves were obtained by plotting the blood-sugar figures. In the majority of cases (70 per cent) the curve

rose rapidly to the maximum and at once began to fall to its original level. In 9 per cent of the cases the maximum level was sustained for a longer time, the so-called plateau curve. In 7 per cent of the cases the curve rose slowly reaching its maximum point at the end of ninety to one hundred and twenty minutes and then quickly falling to its original level. In 14 per cent of the cases the curve reached its maximum at the end of one hour, then fell but rose a second time making two peaks in the curve.

Many of these irregularities in the curves may be explained by the observations of Hansen[5] on sugar-tolerance tests in adults. She showed that if the blood sugar is determined every two minutes for two hours the plotted curve is not smooth but that there are distinct oscillations, the blood sugar varying as much as 20 mg. from minute to minute, and that the greatest variations take place at the plateau portion of the curve. These oscillations may affect the accurate estimation of the highest and lowest points of the blood-sugar curve when blood-sugar determinations are made at thirty minute intervals. They would also explain the apparent but possibly not real differences in the blood-sugar curves of the same individual on two different days. Blood-sugar determinations taken every thirty minutes, however, give a fairly accurate picture of the true blood-sugar curve.

The blood sugar in the fasting state ranged from 90 mg. to 130 mg., the average being 108 mg. per 100 cc. of blood. This amount is in agreement with the findings of others who used the same method. A few of the children cried with fear while the blood was taken, a mental state which according to Folin and Berglund[6] may cause a rise in the blood sugar. Hansen[5] has shown, however, that the blood sugar of a normal fasting adult may vary 20 mg. within one hour's time.

After ingestion of glucose, the blood sugar reached its maximum height within an hour in 90 per cent of the cases as noted by other investigators. Although the average maximum was 180 mg. of glucose per 100 cc. of blood, nevertheless in 20 per cent of the cases it rose above 200 mg. This high level was reached, not only in cases where large amounts of sugar were given, but also in a few cases where small amounts were administered. The average maximum in the obese children was 190 mg. per 100 of blood as compared to 178 mg. in the normal and underweight. The blood sugar of children between seven and ten years of age reached a higher average level than those younger than seven and older than ten years of age.

Fourteen cases were tested on two different days. Thirteen received different amounts of sugar on the two days, and 1 case the same amount. The fasting level in the same child varied from day to day, the average variation being 12 mg. per 100 cc. of blood, the maximum being 25 mg. per 100 cc. of blood. In 1 case the tolerance was better on one day than on another; that is, although the child

received a greater amount of sugar than on the previous day, the fasting level was reached in a shorter period of time. In 1 case where the same amount of sugar was given on two successive days the type of curve was different, although the fasting level was reached in the same period of time.

Testing the urine for sugar with Fehling's reagent in these normal children proved of little value, as this reagent is sensitive only to amounts of glucose greater than 0.1 per cent, a quantity rarely excreted by normal individuals with blood sugar below 180 mg. per 100 cc. of blood. In only 20 per cent of cases did the blood sugar rise above 180 mg. Hansen,[5] Folin,[6] and others, have shown in normal adults that no matter how large the amount of sugar given, the blood sugar only occasionally rises above 180 mg. per 100 cc. of blood.

In this series of cases, where the blood sugar remained below 160 mg. no positive Fehling's reaction was obtained. A positive reaction was obtained in one third of the cases, when the blood sugar ranged from 160 to 200 mg. per 100 cc. of blood. When the blood sugar was over 200 mg., a positive reaction was usually obtained in the urine. Whenever the reaction was doubtful or positive, a confirmatory yeast fermentation test was made.

Summary. 1. Eighty-four normal children from three to thirteen years of age were given varying amounts of glucose by mouth. Fourteen were tested a second time, making 98 tests in all. Blood-sugar determinations were made before the ingestion of the glucose and thereafter every half hour for two hours, including a final determination after three hours. The urine was tested with Fehling's reagent for glucose.

2. In children receiving less than 2 gm. of glucose per kilo of body weight, the blood sugar returned to the fasting level in 83 per cent of the cases at the end of three hours. When more than 2 gm. of glucose per kilo of body weight was given, 64 per cent of the cases reached the fasting level within three hours.

3. For less than 2 gm. of sugar per kilo of body weight, the tolerance is the same for children of all ages. Of children between three and six years, 96 per cent can tolerate 2 to 2.9 gm. per kilo of body weight, while only 43 per cent of the older children can tolerate this amount. The children between seven and ten years of age, appear to have a poorer tolerance for the larger amounts of glucose, than those younger than seven and older than ten.

4. The state of nutrition does not appreciably affect the sugar tolerance of children from three to six years. In children over six years of age, 77 per cent of the underweight and normal weight can tolerate less than 2.0 gm. of glucose per kilo of body weight, whereas in the overweight only 45 per cent can do so. The tolerance of all the older children for over 2 gm. per kilo of body weight is very poor, regardless of the state of nutrition.

5. Four distinct types of blood-sugar curves were obtained.

6. The fasting blood sugar ranged from 90 mg. to 130 mg. per 100 cc. of blood; the average being 108 mg.

7. The blood sugar in 90 per cent of the cases reached its maximum within an hour after the ingestion of the glucose. The average maximum was 180 mg. per 100 cc. of blood. In 20 per cent of the cases the blood sugar rose above 200 mg. at some time during the test.

8. Fourteen cases were tested on two different days. The fasting level and type of curve of the same child varied from day to day. In 1 case the tolerance was better on one day than on another.

9. Testing the urine for glucose with Fehling's solution is of little value in normal children as a test for glucose tolerance.

Conclusions. 1. The most satisfactory amount of glucose for testing the glucose tolerance of children from three to thirteen years of age, within a period of three hours, is 1.5 to 2 gm. per kilo of body weight.

2. Many normal children do not return to the fasting level at the end of three hours.

3. The younger children have a better tolerance than the older for larger amounts.

4. Children from seven to ten years of age apparently have the poorest tolerance.

5. The state of nutrition has no effect on the tolerance of the younger children.

6. The overweight older children have a lower tolerance when the glucose is given according to body weight.

7. The fasting level, tolerance and type of curve of the same child may vary from day to day.

II. **Glucose Tolerance in Relation to Nutritional Surface and Body Surface.** In the foregoing, the results of glucose tolerance tests in children were described. The amount of glucose administered depended on the weight of the child. The question arose as to the accuracy of this method, as it has been long recognized that all metabolic processes bear a more constant relationship to the surface area than to the weight. The difficulty in determining the surface area has up to the present been an obstacle in using it as a basis for calculation in testing sugar tolerance.

One of the first methods used for the determination of the body surface was the Meeh-Vierordt formula, (S.A. = 12.3 $W^{\frac{2}{3}}$). This was later modified by Lissauer. Benedict and Talbot[7] determined another constant for this formula for normal children of different weights and believe this modification to be more satisfactory. The formula used by Benedict and Talbot does not give the real body surface, but its value depends on its relationship to the two-thirds power of the weight. Another formula now in general

use is that of Du Bois which takes into consideration not only the weight but also the height of the individual. In the same category is the Pirquet nutritional surface which is calculated by squaring the sitting height. Pirquet[8] found that the sitting height cubed is equivalent to ten times the weight.

$$\begin{aligned} Si &= \text{Sitting height} \\ W &= \text{Weight.} \\ Si^3 &= 10\ W \\ Si &= \sqrt[3]{10\ W} \\ Si^2 &= (\sqrt[3]{10\ W})^2 \end{aligned}$$

The sitting height squared, therefore, is also in relation to the two thirds power of the weight.

Using this latter formula the nutritional surface area can easily be determined by squaring the sitting height. The total calories or as Pirquet prefers to say, milk units, required per square meter of body surface can be calculated very readily. The terminology of Pirquet follows:

1 gm. milk value equals 1 nem.
0.1 gm. milk value equals 1 decinem.
1 gm. sugar is equivalent to 6 milk values or 6 nem.
0.017 gm. sugar equals 0.1 gm. milk value or 1 decinem.

In order to bring the amount of glucose into relationship to the Pirquet nutritional surface, the sitting height instead of the body weight, was used as the unit of measurement. No new tests were carried out. The grams of glucose per kilo body weight were calculated in relation to the nutritional surface and then expressed in terms of decinem.

At first 0.017 gm. of glucose or 1 decinem was given for each square centimeter of the sitting height squared, and in no case did the blood sugar return to the fasting level in three hours. Therefore, less than this was given, namely, 0.013 gm. of glucose (0.75 decinem) and 0.0085 gm. of glucose (0.5 decinem) per square centimeter of the sitting height squared. Only the results of this second group of cases were tabulated.

This calculation can be seen more readily from the following example:

A child has a sitting height of 60 cm. $Si^2\ (60 \times 60) = 3600\ cm.^2$

If we wish to give 0.75 decinem for each square centimeter of sitting height squared we multiply 3600×0.75 which equals 270 nem (milk value).

Since 1 gm. of sugar is equal to 6 nem one may, by dividing 270 by 6, obtain the total grams of sugar for the test.

$$(270 \div 6 = 45 \text{ gm. of sugar})$$

If another child of the same sitting height were given 0.5 decinem, the calculation would read: $3600 \times 0.5 = 180$ nem (milk value); $180 \div 6 = 30$ gm. of sugar.

Taking the amount of sugar as determined by the above calculation and dividing this amount by the weight of the child, it was found that 0.75 decinem of sugar was equivalent to 2.1 to 2.8 gm. of glucose per kilo of body weight and 0.5 decinem to 1.5 to 1.8 gm. per kilo of body weight. These comparisons should only be made in cases of normal nutrition. As previously stated it is customary to give normal adults from 1.5 to 1.8 gm. of glucose per kilo of body weight which is therefore the equivalent of 0.5 decinem in children.

TABLE IV.—TOLERANCE FOR VARYING AMOUNTS OF GLUCOSE PER SQUARE CENTIMETER OF SITTING HEIGHT SQUARED.

Glucose per sq. cm. sitting height squared.		End of 2 hours.			End of 3 hours.		
Decinem.	Grams.	Total cases.	Returned to fasting level.		Total cases.	Returned to fasting level.	
			Cases.	Per cent.		Cases.	Per cent.
0.5	0.0085	53	21	40	53	44	83
0.75	0.0130	38	13	34	33	22	66

The glucose tolerance of all children regardless of age for 0.75 decinem and 0.5 decinem of glucose has been tabluated in Table IV.* When 0.75 decinem was given, the blood sugar of only 34 per cent of the cases returned to the fasting level at the end of two hours, and 32 per cent more returned to the normal at the end of three hours, a total of 66 per cent returning to the fasting level at the end of three hours. When 0.5 decinem was given, 40 per cent of the cases returned to the fasting level at the end of two hours, and 44 per cent more at the end of three hours, a total of 83 per cent returning to the fasting level at the end of three hours. This fact was noted in the first part of the paper, namely, that only 83 per cent of children can tolerate less than 2 gm. of glucose per kilo of body weight which is the equivalent of 0.5 decinem in the normal state of nutrition.

The glucose tolerance in relation to the age of the children can be seen from Table V. When 0.5 decinem is given the tolerance is the same for all ages. When 0.75 decinem is given the tolerance of older children is not as good as that of the younger children. The children between seven and ten years receiving 0.75 decinem have a poorer tolerance than those older than ten and younger than seven.

* For practical purposes those cases whose blood sugar returned within 15 mgm. of the fasting level, were included in the total percentage.

TABLE V.—TOLERANCE IN RELATION TO AGE AND AMOUNT OF GLUCOSE PER SQUARE CENTIMETER OF SITTING HEIGHT SQUARED.

Age, yrs.	Glucose per sq. cm. sitting height squared.		End of 2 hours.			End of 3 hours.		
	Decinem.	Grams.	Total cases.	Returned to fasting level.		Total cases.	Returned to fasting level.	
				Cases.	Per cent.		Cases.	Per cent.
3 to 6	0.50	0.0085	24	9	36	24	20	83
	0.75	0.0130	17	6	35	16	14	86
7 to 9	0.50	0.0085	12	2	17	12	10	84
	0.75	0.0130	10	0	0	8	2	25
10 to 13	0.50	0.0085	17	9	53	17	15	88
	0.75	0.0130	11	3	27	9	5	56

To determine whether the carbohydrate tolerance is affected by the state of nutrition, the children were grouped into 3 classes according to the Pirquet standard.* The relation of the glucose tolerance to the state of nutrition can be seen from Table VI.

I. Underweight: Pirquet index less than 93.
II. Normal weight: Pirquet index of from 93 to 97.
III. Overweight: Pirquet index more than 97.

Pirquet uses the formula $100 \frac{\sqrt[3]{10\ W}}{Si}$ as a nutrition index. Tables have been compiled giving the Pirquet index for varying weights and sitting heights. Austrian school children of a normal state of nutrition have an index of between 93 to 97.

It was of interest to compare this system with that of the Baldwin-Wood Height, Weight, Age Index. None of these nutritional systems are infallible as has been shown by Clark, Sydenstricker and Collins,[9] Baker and Blumenthal,[10] and Dublin and Gebhart.[11] These authors have shown that occasionally a child considered underweight by one standard is normal or in rare instances overweight by another. Not infrequently a physician's clinical diagnosis of the state of nutrition does not agree with the mathematical standard. According to the Pirquet standard 33 per cent of the children tested

* Basis for calculation of Pirquet nutrition standard:

Si = Sitting height
$10\ W$ = Ten times the weight
$Si^3 = 10\ W$
$Si = \sqrt[3]{10\ W}$
$\frac{\sqrt[3]{10\ W}}{Si} = 1$

were underweight and 21 per cent, overweight. If the Pirquet index of 92 had been taken as the lower limit of normal nutrition instead of 93, then 23 per cent of the cases would have been classed as underweight, which was the same percentage obtained when these children were grouped according to the Baldwin-Wood standard.

TABLE VI.—TOLERANCE PER SQUARE CENTIMETER SI^2 IN RELATION TO AGE, AMOUNT OF GLUCOSE, AND STATE OF NUTRITION.

Age, yrs.	Glucose per sq. cm. sitting height squared		Pirquet nutritional index.	End of 2 hours.			End of 3 hours.		
	Decinem.	Grams.		Total cases.	Returned to fasting level.		Total cases.	Returned to fasting level.	
					Cases.	Per cent.		Cases.	Per cent.
3 to 6	0.50	0.0085	−93	7	3	44	7	4	66
			93 to 97	13	9	70	13	12	92
			98+	4	0	0	4	4	100
	0.75	0.0130	−93	3	1	33	3	3	100
			93 to 97	10	4	40	9	9	100
			98+	4	1	25	4	3	75
7 to 13	0.50	0.0085	−93	13	5	38	13	11	84
			93 to 97	12	5	42	12	11	92
			98+	4	2	50	4	2	50
	0.75	0.0130	−93	5	1	20	5	3	60
			93 to 97	8	0	0	7	2	29
			98+	8	2	5	5	3	60

When taking into consideration the age of the child concomitantly with the Pirquet nutrition index as shown in Table VI, there is practically no difference in the tolerance for 0.5 decinem in younger and older children, regardless of their state of nutrition. When 0.75 decinem is given to the younger children the blood sugar of the underweight and normal ones returns to the fasting level within the time limits of the test. There are too few young obese individuals to make any definite statement. In the older children 0.75 decinem is apparently too much, regardless of the state of nutrition. From Table VI the normal older children receiving 0.75 decinem appear to have a lower tolerance, but this fact is a result of the chance inclusion of the children between seven and ten years of age who were previously shown to have a poorer tolerance.

As noted in Part I, when the amount of glucose given was in relation to the body weight, the older overweight children had a lowered sugar tolerance. But this was not true when the amount of glucose administered was in relation to Pirquet nutritional surface. When this latter method was used the tolerance of under-

weight, normal—and overweight children was approximately the same. This is readily understood when it is considered that the sitting height, which is used as the basis of calculation, is a linear measurement and is the third root of the expected weight and not of the actual weight. Therefore, the amounts given are independent of the state of nutrition, which is not the case when the amount of glucose is based on the body weight. This fact is brought out clearly in Table VII where 0.5 decinem is expressed in terms of grams per kilo for the two age groups of different states of nutrition. The younger and more underweight a child is, the larger is the amount given in terms of grams per kilo of body weight; the older and heavier, the less glucose does it receive per kilo of body weight.

TABLE VII.—EFFECT OF AGE AND NUTRITIONAL CONDITION OF CHILDREN ON GLUCOSE DOSAGE USING PIRQUET SYSTEM.

Age, yrs.	Pirquet index.	Glucose per sq. cm. sitting height squared.		Average grams per kilo body weight.
		Decinem.	Grams.	
3 to 6	93	0.5	0.0085	1.85
	93 to 97	..	..	1.66
	98+	..	..	1.60
7 to 13	−93	0.5	0.0085	1.58
	93 to 97	..	..	1.50
	98+	..	..	1.20

Comparing two children of the same sitting height, a heavy child may receive as much as 0.5 gm. less per kilo than a thin child. Therefore, calculating the amount of glucose for a tolerance test the amount of surface area instead of weight is more satisfactory.

Table VIII gives the details of all the examinations upon which this article is based.

Summary. 1. In Part I of this paper, the amount of glucose administered was calculated from the body weight of the child; in Part II, the amount of glucose was calculated in relation to the nutritional surface of the child. The Pirquet nutritional surface was used, the sitting height being the unit of measurement. The amounts of glucose given are expressed in terms of decinem.

2. In those cases receiving 0.5 decinem of glucose, in 83 per cent of the cases the blood sugar returned to the fasting level at the end of three hours, and in those receiving 0.75 decinem 66 per cent of cases returned to the fasting level in three hours.

3. The tolerance of children of all ages is the same for 0.5 decinem of glucose. When given 0.75 decinem, 86 per cent of the children between three and six years, 25 per cent of the children from seven to nine years, and 56 per cent of the children from ten to thirteen years returned to the fasting level in three hours.

TABLE VIII.

Case No.	Age.	Sex.	Weight, kilo.	Length, cm.	Sitting height, cm.	Body surface, (DuBois-Linear), sq. m.	Nutritional index.		Glucose.			Blood-sugar percentage.					
							Variation from Baldwin-Wood.	Pirquet.	Grams per kilo body weight.	Decinem per Cm^2 per Si^2.	Grams per sq. m. body surface.	Fasting.	30 minutes.	60 minutes.	90 minutes.	120 minutes.	180 minutes.
*88	3	M.	16.0	98	57	0.64	0	96	1.50	0.50	42	0.115	0.160	0.150	0.120	0.105	0.110
*86	3	M.	16.0	98	57	0.64	0	96	2.00	0.65	50	0.100	0.200	0.170	0.180	0.160	0.100
70	3	M.	14.5	92	56	..	0	94	1.70	0.50	..	0.105	0.170	0.177	0.112	0.125	0.108
77	3	M.	13.5	88	52	..	+ 2	98	2.00	0.50	..	0.130	0.210	0.180	0.250	0.150	0.100
32	3	F.	16.7	102	59	0.70	+ 1	95	2.50	0.75	61	0.090	0.190	0.170	0.120	0.090	0.090
43	3	M.	16.0	96	56	0.65	+ 4	95	2.55	0.75	65	0.108	0.200	0.160	0.130	0.105	0.120
31	3	F.	13.0	88	52	..	+ 2	98	2.60	0.75	...	0.095	0.200	..	0.160	0.105	0.105
*63	4	M.	18.6	110	63	0.77	0	91	1.50	0.40	35	0.130	0.220	0.240	0.244	0.250	0.190
*58	4	M.	18.6	110	63	0.77	0	91	1.80	0.50	43	0.085	0.110	0.180	0.220	0.160	0.190
91	4	M.	18.2	98	57	0.69	+16	99	1.50	0.50	39	0.107	0.164	0.160	0.185	0.140	0.100
39	4	F.	26.0	100	58	0.78	+35	110	1.60	0.75	54	0.095	0.200	0.220	0.200	0.145	0.145
*33	4	F.	14.0	90	53	..	− 1	98	1.70	0.50	..	0.095	0.190	0.175	0.130	0.120	0.095
*30	4	F.	14.0	90	53	..	− 1	98	2.50	0.75	..	0.100	0.150	..	0.250	0.170	0.120
92	4	M.	15.5	98	57	0.65	− 2	94	1.70	0.50	41½	0.110	0.180	0.180	0.180	0.140	0.105
72	4	M.	15.5	92	54	0.60	+15	100	2.00	0.65	50	0.120	0.190	0.176	0.180	0.220	0.130
76	4	M.	15.2	94	55	0.60	0	97	2.00	0.60	50	0.125	0.180	0.140	0.150	0.125	0.125
23	4	M.	17.1	94	55	0.60	+11	101	2.30	0.75	65	0.110	0.140	0.170	0.150	0.160	0.135
20	4	M.	15.4	92	54	0.60	+15	100	2.40	0.75	59	0.115	0.120	0.150	0.170	0.190	0.102
99	4	M.	18.0	104	60	0.70	+ 1	95	2.50	0.75	65	0.110	..	0.160	0.184	0.170	0.110
42	4	F.	16.0	98	57	0.65	− 1	96	2.50	0.75	63	0.120	0.180	0.130	..	0.140	0.110
18	4	M.	15.9	105	60	0.68	−12	91	2.80	0.75	66	0.117	0.200	0.186	0.150	0.200	0.120
11	4	M.	15.4	102	58	0.67	0	93	2.90	0.75	59	0.105	0.160	0.164	0.174	0.160	
56	5	F.	16.8	97	57	0.67	+ 8	97	1.60	0.50	41	0.100	0.130	0.140	0.120	0.100	0.100
74	5	M.	19.1	92	63	0.73	0	92	1.60	0.50	43	0.125	0.190	0.148	0.170	0.150	0.160
*73	5	M.	20.4	108	62	0.77	+ 8	95	1.70	0.50	47	0.110	0.190	0.170	0.170	0.125	0.125
*75	5	M.	20.4	109	62	0.76	+ 8	95	2.00	0.60	52	0.120	0.190	0.170	0.184	0.154	0.600
*54	5	F.	17.5	106	60	0.72	+ 6	94	2.00	0.60	50	0.120	0.190	0.200	0.135	0.130	0.100
*50	5	F.	17.5	106	60	0.72	+ 6	94	2.00	0.60	50	0.080	0.152	0.160	0.180	0.130	0.100
*53	5	M.	18.6	108	61	0.74	− 2	94	2.00	0.60	50	0.115	0.185	0.130	0.140	0.125	0.135
*57	5	M.	18.2	108	61	0.74	− 3	94	1.70	0.50	43	0.096	0.200	0.150	0.150	0.108	0.090
29	5	M.	18.6	108	61	0.74	− 4	94	2.20	0.70	57	0.095	0.175	0.160	0.180	0.160	0.120
14	5	M.	18.6	102	59	0.70	+ 6	97	2.30	0.75	62	0.125	0.240	0.180	0.178	0.170	0.125

57	5	M.	18.2	108	61	0.74	− 3	94	1.70	0.50	43	0.096	0.200	0.150	0.150	0.108	0.090
29	5	M.	18.6	108	61	0.74	− 4	94	2.20	0.70	57	0.095	0.175	0.160	0.180	0.160	0.120
14	5	M.	18.6	102	59	0.70	+ 6	97	2.30	0.75	62	0.125	0.240	0.180	0.178	0.170	0.125
35	5	M.	15.7	100	57	0.65	− 2	95	2.60	0.75	63	0.100	0.190	0.150	..	0.170	0.110
64	6	F.	18.0	110	62	0.74	−10	92	1.50	0.40	36	0.120	0.180	0.170	0.140	0.130	0.090
60	6	F.	17.7	110	62	0.74	−11	91	1.80	0.50	43	0.115	0.135	0.180	0.190	0.140	0.105
79	6	M.	20.4	112	62	0.80	− 1	95	1.60	0.50	38	0.103	0.140	0.135	0.120	0.170	0.122
59	6	M.	16.4	108	61	0.70	−14	90	1.90	0.50	44	0.100	0.180	0.180	0.160	0.105	0.090
28	6	F.	16.3	109	61	0.70	−20	89	2.50	0.65	60	0.110	0.220	0.180	0.160	0.128	0.110
100	6	M.	21.0	120	67	0.85	−11	89	2.60	0.75	65	0.100	0.160	0.156	0.110	0.100	0.100
102	6	F.	18.0	106	61	0.75	0	93	2.60	0.75	60	0.110	0.170	0.160	0.135	0.120	0.125
93	6	M.	17.5	106	60	0.70	−12	90	2.90	0.75	64	0.100	0.160	0.180	0.156	0.154	0.120
2	6	M.	21.4	122	66	0.85	−17	88	4.40	1.00	102	0.125	0.220	0.231	0.210	0.220	
61	7	F.	20.0	108	61	0.75	+ 6	96	1.60	0.50	43	0.106	0.130	0.195	0.190	0.145	0.105
27	7	M.	21.3	114	65	0.80	+ 2	93	1.65	0.50	44	0.110	0.150	0.230	0.190	0.190	0.120
96	7	F.	32.3	128	71	1.05	+16	97	1.95	0.75	60	0.130	0.175	0.180	0.200	0.184	0.130
51	7	F.	20.9	116	65	0.82	−10	92	2.00	0.60	51	0.115	..	0.165	0.175	0.165	0.115
7	7	M.	25.6	120	66.7	0.90	+ 6	97	2.10	0.75	60	0.118	0.230	0.230	0.198	0.180	
8	7	F.	21.3	120	66	0.83	−10	91	2.10	0.75	56	0.115	0.200	0.200	0.200	0.170	
104	7	M.	23.2	122	68	0.88	− 7	91	2.50	0.75	67	0.092	0.164	0.170	0.110	0.200	0.130
106	7	M.	19.4	112	63	0.78	−10	91	2.60	0.75	64	0.100	0.170	0.180	0.190	0.160	0.110
24	8	M.	33.0	128	70	1.06	+18	98	1.25	0.50	39	0.120	0.230	0.200	0.160	0.125	0.102
89	8	M.	32.3	130	71	1.05	+ 9	97	1.30	0.50	40	0.110	0.240	0.220	..	0.200	0.160
22	8	F.	23.6	122	67	0.90	− 2	93	1.66	0.50	43	0.110	0.200	0.142	0.160	0.170	0.125
21	8	F.	12.7	106	60	0.75	− 5	94	1.80	0.50	40	0.090	0.180	0.160	0.160	0.150	0.115
55	8	M.	22.0	120	66	0.85	−10	92	1.90	0.60	51	0.130	0.185	0.200	0.180	0.155	0.100
101	8	M.	26.4	120	67	0.92	+ 6	96	2.20	0.75	64	0.110	..	0.250	0.220	0.160	0.160
13	8	M.	23.2	122	67	0.89	− 7	92	2.50	0.75	62	0.125	0.190	..	0.220	0.180	0.180
94	8	F.	17.3	104	58	0.70	− 4	95	2.50	0.75	61	0.125	0.170	0.194	0.192	0.156	0.156
1	8	F.	21.8	120	66	0.85	− 8	91	3.30	1.00	86	0.125	0.250	0.210	0.210	0.210	
36	9	M.	50.0	144	77	1.44	+27	103	1.50	0.75	52	0.105	0.240	0.240	..	0.200	0.160
37	9	M.	50.0	144	77	1.44	+27	103	1.10	0.50	31	0.130	0.250	0.140	0.200	0.135	0.100
26	9	M.	30.0	134	73	1.05	− 1	92	1.50	0.50	42	0.098	0.184	0.260	0.200	0.190	0.130
41	9	M.	26.0	130	71	1.00	−11	90	1.60	0.50	42	0.115	0.145	0.178	..	0.160	0.105
105	9	M.	31.4	130	70	1.05	+ 9	98	1.90	0.75	57	0.095	0.100	0.130	0.140	0.150	0.110
95	9	F.	23.6	120	66	0.90	0	94	2.30	0.75	60	0.100	0.170	0.160	0.180	0.180	0.160
40	10	M.	28.8	130	70	1.10	− 2	94	1.40	0.50	37	0.126	0.200	0.180	0.115	0.120	0.100
52	10	F.	27.7	128	70	1.00	− 5	93	1.50	0.50	41	0.130	0.180	0.140	0.155	0.130	0.100
82	10	F.	28.6	134	72	1.03	− 4	92	1.50	0.50	42	0.130	0.180	0.224	0.220	0.125	0.085
83	10	M.	28.0	134	73	1.04	−14	90	1.55	0.50	40	0.095	0.200	..	0.180	0.170	0.105
5	10	M.	29.0	128	69	1.08	+ 6	98	2.00	0.75	54	0.125	0.216	0.155	0.122	0.136	
107	10	M.	44.0	144	77	1.30	+24	103	1.80	0.75	56	0.110	0.162	0.160	0.156	0.160	0.160
108	10	M.	44.0	144	77	1.30	+24	103	1.10	0.50	35	0.106	0.130	0.160	0.140	0.142	0.140

* Cases in brackets represent the same child tested on two different days.

TABLE VIII.—(*Continued.*)

Case No.	Age.	Sex.	Weight, kilo.	Length, cm.	Sitting height, cm.	Body surface, (DuBois-Linear), sq. m.	Nutritional index.		Glucose.			Blood-sugar percentage.					
							Variation from Baldwin-Wood.	Pirquet.	Grams per kilo body weight.	Decinem per Cm^2 per Sit.	Grams per sq. m. body surface.	Fasting.	30 minutes.	60 minutes.	90 minutes.	120 minutes.	180 minutes.
90	10	M.	24.4	124	67	0.91	− 5	94	2.00	0.75	55	0.120	0.188	0.150	0.134	0.164	0.124
17	10	M.	24.2	122	66	0.91	+ 1	95	2.20	0.75	59	0.130	0.184	0.160	0.190	0.180	0.170
97	10	M.	22.7	122	67	0.89	− 9	91	2.35	0.75	62	0.120	0.246	0.290	0.220	0.200	0.164
3	10	F.	30.0	136	73.5	1.07	− 7	92	3.00	1.00	83	0.112	0.240	0.240	0.240	0.180	
*84	11	M.	30.0	138	74	1.08	− 9	91	1.50	0.50	42	0.105	0.175	0.140	0.130	0.165	0.110
*87	11	M.	30.0	138	74	1.08	−19	91	1.80	0.60	50	0.110	0.170	0.194	0.170	0.148	0.096
*80	11	F.	27.3	122	71	0.95	+10	92	1.50	0.50	44	0.090	0.130	0.135	0.120	0.108	0.108
*81	11	F.	27.2	122	71	0.95	+10	92	1.80	0.60	50	0.103	0.115	0.160	0.170	0.124	0.120
10	11	F.	45.0	144	78	1.32	+14	99	1.60	0.75	58	0.127	0.170	0.220	0.204	0.186	
85	11	M.	28.0	122	71	0.95	+10	93	1.70	0.60	50	0.110	0.180	0.180	0.180	0.115	0.110
98	11	M.	38.0	138	74	1.20	+11	98	1.80	0.75	57	0.120	0.210	0.210	0.180	0.180	0.140
6	11	M.	29.0	124	69	0.93	+10	98	2.00	0.75	59	0.125	0.240	0.240	0.190	0.155	
15	11	F.	19.5	112	61	0.87	− 8	95	2.40	0.75	54	0.120	0.190	0.200	0.210	0.190	0.145
16	11	F.	24.5	120	70	0.95	−19	90	2.50	0.75	64	0.125	0.168	0.115	0.124	0.120	0.110
*46	12	M.	35.2	136	73	1.17	+ 9	97	0.80	0.33	25	0.120	0.110	..	0.125	0.130	0.110
*48	12	M.	36.0	136	73	1.17	+ 9	97	1.20	0.50	38	0.120	0.110	0.130	0.160	0.115	0.110
62	12	F.	47.3	146	78	1.39	+15	100	1.10	0.50	37	0.110	0.190	0.160	0.160	0.150	0.135
*45	12	M.	41.0	144	77	1.27	+ 7	97	0.90	0.33	26	0.112	0.240	..	0.120	0.120	0.120
*49	12	M.	41.0	144	77	1.27	+ 7	97	1.20	0.50	38	0.110	0.130	0.155	0.150	0.140	0.090
65	12	M.	37.3	140	75	1.20	+ 5	96	1.25	0.50	39	0.120	0.200	0.140	0.130	0.120	0.125
78	12	M.	30.0	128	74	1.05	0	91	1.50	0.50	42	0.098	0.168	0.150	0.155	0.140	0.102
103	12	M.	30.0	128	69	1.05	+ 1	99	2.00	0.75	56	0.100	0.210	0.190	0.110	0.110	0.100
4	12	M.	35.0	142	76	1.18	− 4	92	2.70	1.00	82	0.130	0.194	0.190	0.180	0.190	
*34	13	M.	21.0	128	69	0.50	−25	86	1.80	0.50	44	0.120	0.175	0.160	0.184	0.184	0.128
*44	13	M.	22.3	128	69	0.90	−20	89	1.20	0.33	29	0.110	0.120	..	0.135	0.105	0.095
25	13	M.	28.6	122	71	0.98	+10	93	1.50	0.50	44	0.130	0.184	0.210	0.180	0.200	0.120

* Cases in brackets represent the same child tested on two different days.

4. In using the sitting height squared as the unit for calculation, the state of nutrition plays no role and therefore can be disregarded.

Conclusions. 1. When using the Pirquet nutritional surface for calculating the amount of glucose to be administered, 0.5 decinem of glucose is the most satisfactory amount to give to children aged three to thirteen years.

2. Children of all ages have the same tolerance for 0.5 decinem of glucose per square centimeter of sitting height squared.

3. The younger children have a better tolerance than the older ones when more than 0.5 decinem is given.

4. Since in a child of normal weight 0.5 decinem is equivalent to 1.5 to 1.8 gm. of glucose per kilo of body weight, it is immaterial whether the glucose is calculated from the body weight or the nutritional surface.

5. It is more accurate to calculate the amount of glucose from the nutritional surface than body weight in the overweight and underweight children.

6. Since the Pirquet formula $Si^2 = (\sqrt[3]{10\ W})^2$ has the similar two-thirds power relation to the weight as the Meeh-Vierordt and Lissauer formulæ, there is no doubt that these latter formulæ could also be used for calculation. Their use however is more difficult, as the calculation of the Pirquet formula needs only the simple squaring of the sitting height, whereas the other formulæ necessitate the use of logarithmic tables.

* Cases in brackets represent the same child tested on two different days.

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COMMENTS ON BODY WEIGHT IN RELATION TO HEALTH AND DISEASE.*

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Introduction. I have selected for my address the subject of body weight in relation to health and disease. I realize the breadth of this theme, and will, therefore, confine my remarks to certain significant phases of the subject as they bear on the problem of clinical medicine.

The measurement of body weight and its practical importance is an evolution in the scientific study of nutrition, which dates to the sixteenth century, when that great investigator, Lavoisier,[1] applied the quantitative method to the study of chemistry. The marked strides of the past two decades, made in the field of the metabolic disease, are founded on the investigations of the nineteenth century continental observers, starting with François Magendie, followed by Liebig, Voit, and Rubner, and carried forward in our own country by that able band of scientists, dominated particularly by the researches of Lusk, Benedict, Du Bois and McCollum.

Preliminary Physiological Considerations. Before discussing in detail the unusual deviations from the normal body weight, I should like to direct attention to some of the fundamental physiological mechanisms which control weight variation, as observed in the human organism. We all recognize that individuals normally have a tendency to maintain a certain average body weight. The essential factor in the maintenance of this constant level is brought about by the regular intake of water and food. Variation in the water content of the body is a well-known cause of alteration in weight, and is particularly noted after strenuous exercise, or it may be associated with disease, in which the water balance is disturbed. This is commonly seen in nephritis and diabetes.

The body energy is supplied primarily by food. The potential energy of the food absorbed is liberated in the metabolism and leaves the organism as heat. If the amount of energy available to the body in the food absorbed is greater than the amount lost from the body, the excess is stored in the tissues in the form of combustible materials, as proteins, carbohydrates, and fat. The capacity of the body to store protein and carbohydrate is limited, however, so that any considerable storage of excess energy is accomplished by a deposit of fat. On the other hand, if the energy liberated during the metabolism exceeds that which is available in the food absorbed, the deficiency is supplied by a combustion of the

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energy-containing material stored in the body. Eventually, this means a consumption of fat.

The body also possesses a mechanism that operates to prevent wide fluctuations in weight, which might follow changes in the habits of the individual. This adjustment lies in the alteration in the rate of combustion to conform to the food intake, and also by an alteration in the food intake, to meet the energy needs of the organism. Following the intake of food there is a temporary rise in the combustion. This effect is more marked after the consumption of protein, though to a less extent after carbohydrate and fat. The marked rise in the combustion following high protein intake is an interesting phenomenon, first noted experimentally in 1852 by Bidder and Schmidt, (McCollum[2]) and later studied more carefully by Rubner, who termed it the specific dynamic action of protein. Recent studies of Lusk, (1915[3]) indicate that the specific dynamic action of protein is caused by a stimulative effect of specific amino-acids on the oxidative processes of the organism.[4]

In summary then, we may say, with regard to the chief physiological mechanism controlling body weight, that in the normal individual the weight appears to be maintained primarily through an adjustment of food intake to the body needs. The adjustment of the rate of metabolism to correspond with food intake probably becomes an important factor only under unusual conditions.

Standards of Normal or Ideal Weight. Various formulæ have been devised for the estimation of normal weight of persons of different height, sex, and age. In practice it cannot be said that any of these standards have been entirely satisfactory when applied to unselected clinical cases. This handicap of uncertainty, with regard to normal or ideal weight, has been very obvious to those who have dealt with metabolic disease, where it is often necessary to estimate an ideal weight for a given individual.

The difficulty has arisen because of the great number of variable factors which must be taken into consideration, when such a standard is applied. A truly comprehensive formula must take into consideration the following factors: age, height, sex and body build. The numerous insurance tables, based on determinations made on applicants for life insurance, are derived from age, height, and sex; body build is entirely ignored.

In my experience, perhaps the most comprehensive prediction tables available for the estimation of normal weight, are those devised by Dreyer[5] in England during the World War. In his attempt to work out a method for the assessment of physical fitness, he formulated tables from which the normal or ideal weight can be ascertained by using the physical measurements of weight, length of trunk, and chest circumference. With this method the important factor of body build is given its relative significance; whereas age is disregarded, except that the tables apply only to adults. Dreyer's

method, on the whole, probably represents the most scientific and adequate formula for predicting normal weight we have at our disposal.

Overweight and Obesity. Proceeding now to the discussion of the pathological states of body weight and their relation to disease, I will first direct attention to the condition of overweight or obesity.

Overnutrition is extremely prevalent in America and obesity is one of our most common diseases. Du Bois[6] has recently said: "The large amount of public opinion on this subject is in marked contrast to the small amount of scientific information we have regarding it." This statement is particularly true with regard to our knowledge of the exact biochemical and physiological abnormalities, which all agree, must in the final analysis underlie the problem of obesity. Nevertheless, observations are accumulating, some clinical and some chemical, bearing on this subject.

Obesity has usually been divided into two groups, the simple or exogenous type, presumably due to excessive intake of food combined with too little exercise, and the endogenous type, in which those affected frequently possess a lowered combustive power, associated with a disturbance in the endocrine domain.

Recent investigations by Strouse[7,8,9] and his coworkers on the metabolism of obesity, suggest that there is probably a third type, which he tentatively designates a true constitutional variety. This group is characterized by an inability to lose weight on very low total caloric diets of 600 to 1000 calories a day, even though this intake is maintained over a prolonged period; the basal metabolic rate is found to be consistently within normal limits, but there is a definite tendency to a lowering of the specific dynamic action of protein. This type of individual, therefore, appears to possess a metabolism functioning with an unusual economy and represents a true metabolic anomaly, not associated with an endocrine disturbance or excessive food intake. In other words, it can be differentiated by the foregoing criteria from the exogenous and endogenous groups of the older observers.

To return now for a moment to these last mentioned varieties, the exogenous and the endogenous, I will dismiss them with a few words.

The exogenous is probably the most common type of obesity. In this condition, proper management by the physician with coöperation on the part of the patient, afford striking therapeutic results. The basal metabolic rate in these patients is always within normal limits.[10]

In the endogenous group proper, a frank endocrine etiology is usually apparent. I cannot, however, agree that obesity of this type is particularly frequent in adults, when compared with the great number of cases seen in the other two groups. The cases of adiposity I have studied that can be properly included as strictly endogenous

in origin, can be grouped clinically into three classes, depending upon which ductless gland is involved predominately:

1. The thyrogenous class, concerning which all agree, presents the well known picture of myxedema and is found to have a lowered metabolic rate. The adiposity of myxedema is less constant and striking than the undernutrition seen in hyperthyroidism.

2. The gonad class, which occurs practically only in the postadult age.[11] The justification for distinguishing this variety of adiposity rests on considerable experimental evidence as noted in the effects of castration in animals and man.

3. The hypophyseal class, though striking clinically, in the picture of Fröhlich's syndrome and its modifications, rests on a less secure scientific basis as to its exact nature. The recent work of Smith[12] and Evans[13] on the anterior lobe of the pituitary and that of Abel[14] on the posterior lobe, have added important facts regarding the complex function of this gland, and give promise of finally establishing clinical entities on a real physiological basis.

Speaking generally, it is the endogenous group of adiposities where alterations in the normal metabolic rate can be sought with most optimism, and likewise, in which, organotherapy offers most from the therapeutic standpoint.

With this sketch of our present-day conceptions of the types of obesity, I will pass to a brief consideration of certain diseases which appear to have some relation to the condition of overweight, opening this discussion with diabetes mellitus.

Overweight and Diabetes. The association of overweight and diabetes has long been noted, while in the presence of a wasting disease diabetes is practically unknown. Perhaps we owe more to Joslin and Allen than to other students of this disease, for the stress they have put upon obesity as a frequent prediabetic condition. Joslin[15] states that in 1063 cases of diabetes marked obesity preceded the onset of this disease in more than 40 per cent. The intimate relationship of excess body weight to diabetes is clearly emphasized by the following well known observations.

Reduction in weight in diabetes is associated with marked benefit, as evidenced by a clearing up of the active symptoms, and a gain in the assimilative power. We believe this is related to an increase in the effective mass of active pancreatic islets relative to the size of the individual. On the other hand, a gain in weight is frequently followed by a reduction of the sugar tolerance.

A word at this point about the gain of weight following the use of insulin may not be amiss. The most spectacular increase in weight following insulin occurs in patients suffering marked emaciation, acidosis and dehydration. This prompt increase of weight is associated with changes in the fluid balance, as can be shown by recording the fluid intake and output. It is found that the increase of weight is largely due to fluid retention. The type of diet served

the severe diabetic is rich in mineral salts, and these assist in maintaining a normal osmotic pressure in the tissues so that the patient quickly attains a plump appearance, while the tissue turgor is distinctly increased. The amount of weight increase in emaciated patients due to stored fluid without edema may be astonishing.

Body weight affords a valuable index of the clinical state in this disease, and the diabetic who is maintained at a body weight between normal and 15 per cent below normal, I feel, is in the most satisfactory condition.

All obese patients should be studied with reference to their sugar tolerance as determined by a blood-sugar curve, and a quantitative measurement of urinary sugar and fluid output. I am convinced that further observations of this character will aid in clearing up some of the uncertainties now surrounding the relationship of obesity to diabetes, and further, it will enable us to discover individuals whose lowered sugar tolerance augurs the onset of this disease.

Surgical Aspects of the Obese. I should like to make a plea for the close coöperation of the surgeon and the internist in the management of the obese patient on whom prospective surgery is anticipated. Until recently, patients handicapped thus were regarded as potentially grave surgical risks, and so accepted by the surgeon without due consideration of the possibilities of preoperative preparation and postoperative management.

The obese patient has been recognized as a grave surgical risk for years, not only because of the mechanical difficulty of the operation, but because he is prone to unfortunate complications such as infection, the tardy healing of wounds, and fat embolism.

The preoperative care of the obese will reduce the operative mortality by half. This preparation should aim to reduce the body weight by 10 to 20 per cent by a restriction in the total diet, and especially curtailing the fat and carbohydrate components. A rest period in bed for a week or ten days is also of decided value in obtaining better relaxation of the abdominal musculature.

Ether is probably the anesthetic of choice. Local anesthesia is less satisfactory in the obese than in the ordinary subject, because the infiltration of fatty itssues tends to produce necrosis and retards healing. It must be remembered that the reparative process of tissues is slower in these individuals at best. Surgeons have recognized the peculiarities of healing in the obese and have, therefore, learned that they should be especially careful in handling fatty tissue to prevent trauma, and to reduce manipulation to a minimum. In closing the incision, dead spaces should be particularly avoided.

The postoperative management should aim to prevent pulmonary complications, cardiac failure, wound infection, reopening of the wound, hernia, and fat embolism. Healing should be complete before the patient is allowed up.

Team work between the surgeon and the internist is the keynote to successful surgery in the obese.

Cardiovascular Diseases Including Arterial Hypertension and their Relation to Overweight. I wish to discuss next the association of cardiovascular diseases including arterial hypertension and overweight.

There are three definite conditions, which though in no way part of the general process of obesity, are frequently associated with it, namely coronary sclerosis, hypertension and atrophy of the heart muscle. Needless to say these conditions may occur singly or combined, and are increased in their clinical significance by the presence of a high diaphragm which is a common finding in the obese type of body build.

In the present state of our knowledge, perhaps the most important bearing of obesity to circulatory disease depends upon the general mechanical burden enforced on the cardiovascular system. In younger individuals, without a history of heart damage following infection, and in whom the overweight has been of comparatively recent origin, this handicap is not so apparent; whereas, in the older patients, and particularly those of long-standing obesity, the circulatory complications are of great significance, both in the incapacitating effects and in endangering the prognosis.

I do not wish to dwell at length on the important bearing of overweight to the degenerative cardiovascular diseases, but I should like to add just a word concerning this condition and arterial hypertension.

At the present time we have no scientific proof of an etiological connection between obesity and hypertension, despite the common clinical experience, that reduction in weight is at times followed by a reduction in the systolic blood pressure and marked improvement in subjective symptoms.

Orthopedic Problems and Obesity. I am convinced that any one who sees a number of obese patients will be struck by the prominence of certain orthopedic problems associated with the state of well marked overweight. At least this has been my own experience in the Metabolic Clinic of the Out-patient Department of the University of California Hospital during the past four years. In general it appears to me that these problems are of two kinds however the two groups are not always entirely separable.[16] The first pertains to the association of arthritis in the obese, whereas the second deals more specifically with certain postural and static difficulties, combined with faulty bodily mechanics, seen in these patients.

To consider first the arthritis of the obese, I wish to make it clear from the outset that I am not one of those who believe with Pemberton that arthritis is primarily a metabolic disorder. In my opinion, the weight of evidence at the present time indicates that

arthritis is a problem of physiology and biochemistry, in which infection probably plays the essential, precipitating role. My theme in regard to the association of arthritis and obesity is somewhat as follows: The sedentary habits of the obese predispose to muscular atrophy both in the skeletal and cardiac musculature. This rarely appears before the thirty-fifth year of life. It is not a long stretch of the imagination to assume that joint changes also occur in these individuals, as a comparable degenerative process. With the presence of points of low resistance and possibly disturbed circulation in structures of such anatomy and function as the joints, the soil is prepared for the ready production of local changes of cartilage at the joint margins. Foci of infection can usually be demonstrated in these cases and are probably the precipitating and essential factor in the process, although this point remains unsettled. The arthritis of the obese is usually the hypertrophic or degenerative variety and causes disability from the mechanical irritation of the bony spurs, rather than from an active inflammatory process in the ordinary sense.

From the clinical standpoint, one of the most important groups of cases, is represented by the low back pain of hypertrophic arthritis. This is usually due to strain of a spine in which there is already limitation of motion, and is sometimes precipitated by external trauma. The therapeutic indications in this group comprise improvement of the body mechanics combined with protection of the back by suitable support from further strain and an attempt to arrest the arthritis.

The postural and static difficulties of the obese are common and well recognized and result primarily from faulty bodily mechanics. There is a basic principle, accepted and utilized by the orthopedists, but not so fully appreciated and applied by the internists,[17] that the use of the body in faulty mechanical alignment is always a potential source of trouble. Goldthwait,[18] in the Shattuck Lecture, in 1915, drew attention to the types of body build and their significance in medical disease. The group of individuals prone to develop postural disturbances and hypertrophic arthritis are represented in the so called herbiverous class. The abnormally large and heavy abdominal viscera in these people leads to backward inclination of the body, which produces a strain at the dorsolumbar juncture. The strain thus produced upon the lower back leads to a sensitiveness at the lumbosacral juncture, and in this way, accounts for some cases of lumbago. Another common form of spinal deformity closely allied with the condition just mentioned is scoliosis. The pelvis is apt to be thrown backward at its top asymmetrically, and a lateral curvature follows. This produces the socalled sciatic scoliosis.

The postural strains of the lumbosacral region are more common in heavy women. The pain is nearly always of gradual onset and often follows a period of heavy work or a marked gain in weight.

The location of the pain is characteristic. It is not referred down the thighs or legs, but is bilateral in the low back and most acute in the lumbosacral region. It is not sharp and burning, but is described as a dull ache, or tired feeling, and is usually worse at night. These patients are frequently of the heavy type of body build with a sharp lumbar lordosis. The posture is usually poor, in that they stand with the head forward, shoulders drooped, chest flat, abdomen relaxed, lumbar spine hyperextended, body slumped and the body weight resting upon the heels with the feet pronated. A further condition frequently encountered in these overweight people, is produced by the bulky viscera in the upper abdominal cavity, eventually sagging and stretching the abdominal walls. Ventral hernia and visceroptosis ensue with their train of functional disturbances. Disabilities of the lower extremity result also from excessive weight bearing and the flat foot of middle life, when the figure has become rotund and the muscles flabby, hardly needs to be mentioned.

Undernutrition in Relation to Disease: Some General Remarks. Up to this point, I have outlined in some detail certain pathological states associated with overweight, that have impressed me of clinical interest. I now wish to make a few general remarks on our present day conceptions of the medical aspects of undernutrition and underweight.

An important phenomenon accompanying undernutrition was first demonstrated experimentally in 1906 by Magnus-Levy. He pointed out that there is a great reduction in the heat production, which takes place as an accompaniment of emaciation; in other words, the basal metabolism is lowered. Recently, it has been suggested that undernutrition depresses the whole hormonal system. Tallquist[19] noted a reduction in the incidence of exophthalmic goiter in the latter years of the World War, and attributed this fact to the depressing effect of undernutrition on the thyroid gland.

Another important result of undernutrition following an insufficient diet, is a decrease in the efficiency in the performance of physical labor. This is evidenced by the fact that fatigue comes on more quickly than usual and, closely related with this reduction of physical power, mental apathy toward effort becomes apparent.

Certain mechanical changes take place as a result of the loss of body fat, causing a displacement of the anatomical position of the various organs of the body. In some individuals a loss of the subserous and mesenteric fat produces a condition in which the stomach, kidneys and the intestines are not as firmly held in position as formerly. Displacement of the heart combined with a general visceroptosis eventually follows, with the well-known train of symptoms.

All authorities agree that the undernourished individual is far more susceptible to the sensation of cold than is the wellnourished. As previously pointed out in this paper, protein causes a specific stimulus which increases heat production, whereas, carbohydrate

and fat, when absorbed in excess of the immediate requirements of the body, also cause an additional heat production. In the well-nourished, these factors are protective against the sensation of cold.

Certain important physiological facts in connection with the cardiovascular system have come to light in regard to prolonged undernutrition. Inanition reduces the number of heart beats per minute. Rubner states that in the emaciated there is a slowing of the heart rate to 60, 50, or even 40 beats per minute. The work to be accomplished by the circulation, is naturally not so great as in the wellnourished. This reduction of the burden upon the cardiovascular system is utilized by clinicians in the management of heart disease and arteriosclerosis. Benedict and others have also shown that undernutrition is accompanied by a lowering of both the systolic and the diastolic blood pressure, and this fact can also be utilized favorably, to a certain extent, in the management of essential hypertension.

During the latter part of the World War,[20] German observers noted that the restricted war diet tended to cause a cessation of the menses. This amenorrhea probably depended upon the great reduction of the protein of the diet, and thus represented a protective reaction on the part of the organism. War edema was another interesting form of nutritional disturbance noted in the late war; however, this condition has been described during the famines of war since the Napoleonic era. It occurred in different localities in Europe, and in some districts as high as 9 per cent of the inhabitants were affected. The disturbance appeared after prolonged inanition following diets containing predominately carbohydrate and too little protein. This type of diet tends to favor an accumulation of water in the tissues and was found to be most favorably influenced by rest and a liberal, well-balanced diet.

Undernutrition is a well-known factor in the increased incidence of certain of the infectious diseases. This was clearly shown in Germany with regard to tuberculosis. At the end of the war the death rate from tuberculosis had doubled or had reached the height which it had formerly attained before modern control over its spread had been instituted. The increased susceptibility to cold likewise increased the number of cases of upper respiratory infection and the nontuberculous pulmonary infections. It was also noted that recovery after surgical operations was more difficult. On the other hand, war nutrition, by diminishing the intake of protein and preventing overnutrition, was beneficial to many diabetics.

There are many other important medical phases of undernutrition and underweight which I shall not have time to mention, but with this short survey of some of the outstanding effects of inanition and their bearing on the problems of medicine, I shall pass to the last subject for consideration, the relation of body weight to longevity.

The Relation of Body Weight to Longevity. For knowledge concerning the effect of body weight on the expectation of life, medical men are forced to turn to insurance statistics[21] for the most reliable data available. It is recalled that Oliver Wendell Holmes once suggested that the best recipe that he knew for longevity was to have some chronic minor ailment which one had to take care of and which required a certain amount of solicitude not to overdo things, for such people often proved eminently capable of living on beyond the Psalmist's limit of life. In view of the statistics I am about to present, might it not be well to amend this formula, and and add that people should pay a little more attention to their body weight, aiming to guard against the extremes of both overweight and underweight? In recent years, the life insurance companies have laid more and more stress on the relation of body weight to the mortality rate, and I will epitomize some of their salient findings.

Among short men, that is, those below 5 feet 7 inches in height at the age period forty to forty-four years, an excess of 20 per cent in weight involves an added mortality of 30 per cent above normal. A 40 per cent excess in weight in such individuals, involves an increased mortality of nearly 80 per cent.

Among tall men, those over 5 feet 10 inches in height, the adverse situation is even more marked; for among them, at ages forty to forty-four, a 20 per cent excess in weight carries a 40 per cent increase in the mortality and a 40 per cent excess in weight doubles the mortality.

Underweight presents an entirely different picture. In general, underweight is an advantage, provided of course, the percentage is not too great. Underweight is a serious impairment in early adult life, especially among tall men.

Persons who are 5 feet 10 inches, and who are 20 per cent below the average weight for their height, show an increased mortality of 50 per cent.

Persons 30 per cent underweight have a 50 per cent excess mortality at these early ages. But from the age of forty onward there are apparently no such penalties for underweight, and this condition, in fact, becomes a distinct advantage, for these are the people who have the best mortality rates.

It would seem that the records of insurance companies indicate that there is an optimum weight, that is, a weight-height ratio in relation to age that is associated with the most favorable mortality experience, and that this optimum weight, or best build if you choose to call it, is not the average.

It is stated that those who weigh between 10 and 20 per cent below the average show the optimum condition for longevity at most ages beyond early adult life.

Discrimination must be made between types of build of overweight

persons, it being shown that among overweights having a large chest capacity, the conditions of mortality are more favorable than among those of small chest capacity. Overweights who have large trunks are better risks than those having small chests and large abdominal girths.

On the assumption that the average weight is the best weight, tables of average weights lead to the erroneous supposition that weight should continue to increase with advancing age. While this increase is of very common occurrence, the insurance records indicate that, within certain limits, this excess weight increases the insurance risk and should be carefully avoided.

The records, together with clinical experience, suggest that by restriction in diet and proper indulgence in some form of exercise conditions premonitory of organic impairment and eventual breakdown of the cardiovascular and excretory systems may be averted in many instances. At least they reinforce what hygienists have been advocating for many years and open up to the medical profession a promising field for further investigation in preventive medicine.

Conclusions. From what has been said, I have hoped to emphasize the fact that body weight is a simple measurement of extreme importance in clinical medicine. An individual who presents a marked variation in body weight should demand a rational explanation for this alteration. Our patients should be aware of this fact and unexplained variations in their weight, should incite their curiosity sufficiently to urge them to seek medical advice. Abrupt gain or loss may be explained in certain instances on a physiological basis, but it is more likely to be associated with disease.

The tendency to excessive gain in weight is best controlled in its incipiency. In the majority of adults obesity is of the exogenous type and can be adequately controlled by broad hygienic measures, in which restriction in diet affords only one part of the therapeutic régime. Exceptional instances of the true constitutional type of obesity, recently studied by Strouse, do exist. They represent a true metabolic anomaly which is not entirely understood. Clear cut examples of endocrine obesity are common before the adult age and are believed to be primarily dependent on the disturbance of function of three ductless glands, namely, the thyroid, gonads, and the pituitary, either singly or combined. The endocrines *per se* play a less important part in the obesity occurring in adults.

Aside from the esthetic reasons and the constant inconvenience of marked overweight, this condition should be studiously guarded against, because of the fact that it is found to predispose to diabetes, degenerative cardiovascular diseases, arthritis and static difficulties associated with faulty bodily mechanics.

Surgery in the obese is facilitated and the mortality reduced

if an internist coöperates in the preoperative and postoperative management of these cases.

Loss of body weight and undernutrition have likewise many important medical aspects. Reduction of physical and mental vigor, increased sensibility to cold, depression of the hormonal system, lowering of the metabolic rate, and increased susceptibility to infection are among the most significant results of undernutrition.

Life insurance statistics indicate that those who weigh between 10 and 20 per cent below average, show the optimum condition for longevity at most ages beyond early adult life.

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PHYSICAL DEFECTS AS REVEALED BY PERIODIC HEALTH EXAMINATIONS.

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From the standpoint of individual physical efficiency and the national welfare, it is obviously desirable that the body be kept in the best possible condition to function properly. Minor, and even serious, physical impairments are often overlooked by the individual and this may later result in much personal suffering and needless loss to the community. The results of the army-draft examinations and of a large number of physical examinations of industrial employees and of school children show that this condition is considerably more common than is usually realized. It is essential that indications of physical impairment be discovered early in order that they may be corrected. Interest in this phase of health work has increased as proof has accumulated that impairments are in fact corrected and that other material benefits ensue.

The purpose of this study is not to deal further with the value of physical examinations but rather to present certain facts relative to the physical condition disclosed by those who are examined. In this study, we shall describe the principal findings in a fairly homogeneous group of 16,662 men, policyholders of the Metropolitan Life Insurance Company, examined by the Life Extension Institute in 1921. Apart from the draft examinations, this forms one of the largest groups examined in recent years under uniform conditions. An attempt will also be made to show the significance of certain interrelationships which have long been known to exist between different physical conditions. For example, it has been observed that individuals definitely above normal weight for height and age include a larger proportion who also have high blood pressure than do those whose weights are normal. Likewise, diseases of the vital organs are commonly associated with overweight. Diabetes is recognized as a frequent companion to obesity. We shall not attempt to explain the meaning of all the various interrelationships occurring in the large number of observations tabulated in this report. It seems advisable, however, to submit a somewhat detailed analysis of certain of these factors for the interest which may be derived from such a study.

1. **Source of Data.** At the outset, it should be borne in mind that this is an attempt to describe the condition of a large group of men,

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supposedly able to work, as they appeared for physical examination. Obviously, data assembled in this manner have their limitations, but much effort has been exercised to present a true picture of the situation. The examinations were made by a selected group of medical examiners of the Life Extension Institute (some 8,000 in all) throughout the United States, many of whom were general practitioners new to the standards of health examinations. A fairly large proportion of the examinations (at least 20 per cent) were made by the medical staff of the institute in the New York office. Through field agents and printed instructions to its medical examiners, efforts were made to insure uniformity in the conduct of these examinations. The purpose of the examination, as outlined by the Life Extension Institute, is to determine whether or not the individual is in any way below the best possible condition of health and physical efficiency. It is to be remembered that these examinations differ radically from insurance examinations, for the individuals seeking them are desirous of a complete and thorough health survey and are very ready to disclose impairments both important and trivial in order to obtain advice and later treatment for these conditions.

Uniform reporting cards were used. The examination form is in itself an outline of instruction since it indicates under each question the line of investigation to be followed. The records of these examinations were codified and taken off on anonymous punch cards in the office of the Life Extension Institute. The tabulations of the punch cards and the statistical analysis were made by the Metropolitan Life Insurance Company as a service to the institute and to the public health movement which, we thought, would profit from the results obtained. In no case, could the tabulating office identify the individual policyholder. The strictly confidential nature of the institute's records was recognized at all times, and the statistical tables represent abstracts from the intermediary and impersonal perforated cards only.

During 1921, 18,000 physical examinations of Metropolitan policyholders were made by the institute. But of this number the records of only 16,662 examinations of white males were made available for this study. The rest were cases of females and of colored persons who were not in sufficient numbers to warrant detailed tabular analysis of their records.

The first question which presents itself for consideration is how representative those examined are of the general run of white male policyholders. This question cannot be definitely answered; but a number of points can be made to indicate certain characteristics of this group, which will help to explain some of the findings described later. In the first place those examined show that nearly 60 per cent (59.5) were over the age of thirty-four years, as compared with 53.3 per cent who were above this age in the general run of

ordinary policyholders. It is to be expected that those who seek the benefits of a physical examination would include a larger number of persons at the older ages of life when impairments make themselves more felt and when the question of prolonging life and maintaining working efficiency becomes more absorbing than it is for younger and more vigorous persons.

Unfortunately it has not been possible to secure facts of the occupations followed by this group, but general familiarity with the records, and a test run of the cards, indicated a preponderance of clerical, mercantile and executive pursuits. The regulations of the company have likewise made it much more likely that the groups would be composed of persons in somewhat better economic condition than the general run of policyholders.

If, on the other hand, this group is somewhat better constituted financially than the general run of men, it is to be expected that it is also somewhat more heavily weighted with those who are suffering from physical impairment. The examinations in accordance with the company's offer are entirely optional and it is likely that a proportion of these policyholders either knew or suspected that they were not in good physical condition and were thus more likely to avail themselves of the examination service. It is, therefore, rather difficult to say to what extent the results of the physical examinations to be set forth below show a higher proportion of defects than would be found in the community as a whole or even in the group of ordinary policyholders. But taking it altogether we do not believe that the figures are subject to any marked limitations on this score and that they will be fairly representative of what would be found among any group of 17,000 adult males examined under similar auspices.

2. **Hygienic and Dietetic Habits.** Further light on the composition of this group is thrown by the facts of their hygienic and dietary habits. The chief errors in personal hygiene as viewed by the examining physicians and disclosed among this group are set forth in the table on p. 579.

It is, of course, recognized that comparatively few people follow an ideal diet, and a relatively large number are guilty of errors in personal hygiene. These facts which apply to men classed somewhere above the average among insured groups are of considerable interest from this hygienic standpoint. Our purpose, at this point, is merely to indicate the existing situation on the basis of information obtained by medical examiners and the standard and judgment of the Life Extension Institute. It will be observed that nearly two-fifths (37.6 per cent) of this group showed a high protein intake, about the same proportion (36.9 per cent) consumed too little water, a little more than two-fifths (40.7 per cent) partook of too much tea and coffee; other important errors in diet were observed in nearly one-half (46.6 per cent) of the cases. The use of tobacco in excess was found in one-third of the persons examined (33.1 per cent), and lack of exercise in three-fifths (60.8 per cent).

TABLE I.—NUMBER AND PROPORTION OF PERSONS REPORTING SPECIFIED ERROR IN HYGIENE AMONG WHITE MALE ORDINARY POLICYHOLDERS IN SPECIFIED AGE DIVISIONS.

Personal habits and conditions.	Number of cases.						Percentage of total.					
	All ages.	Under 25.	25 to 34.	35 to 44.	45 to 54.	55 and over.	All ages.	Under 25.	25 to 34.	35 to 44.	45 to 54.	55 and over.
Total persons	16,662	861	5885	5799	3023	1094	100.0	100.0	100.0	100.0	100.0	100.0
Too high protein diet	6,272	337	2274	2140	1149	372	37.6	39.1	38.6	36.9	38.0	34.0
Too little water consumed	6,142	263	2147	2184	1155	393	36.9	30.5	36.5	37.7	38.2	35.9
Too much tea and coffee	6,787	240	2222	2454	1348	523	40.7	27.9	37.8	42.3	44.6	47.8
Other errors in diet	7,766	380	2846	2712	1348	480	46.6	44.1	48.4	46.8	44.6	43.9
Alcohol excessive	111	1	32	37	31	10	0.7	0.1	0.5	0.6	1.0	0.9
Alcohol temperate	1,152	28	352	449	239	84	6.9	3.3	6.0	7.7	7.9	7.7
Tobacco excessive	5,519	239	2108	1923	967	282	33.1	27.8	35.8	33.2	32.0	25.8
Tobacco temperate	2,052	88	688	714	404	158	12.3	10.2	11.7	12.3	13.4	14.4
Hours of work too long	4,407	169	1413	1691	865	269	26.4	19.6	24.0	29.2	28.6	24.6
Lack of exercise	10,126	513	3680	3705	1760	468	60.8	59.6	62.5	63.9	58.2	42.8

3. **Personal and Family History.** With this primary factor of personal habits clearly in mind, it may be well to consider briefly, the family and personal histories with respect to certain important diseases, and then proceed to an analysis of defects discovered upon examination. In nearly 15,000 cases (89.2 per cent) no family history was given of the specified diseases considered important as possible inheritance factors. Some of these policyholders had not filled in the section, others had parents living, and still others reported deaths from causes not tabulated. Of the remaining 10.8 per cent of the cases, 2.6 per cent reported family history of apoplexy or arterial disease, "stroke," cerebral hemorrhage; 2.5 per cent, cancer; 1.6 per cent, tuberculosis; 1.4 per cent, nephritis or Bright's disease; 3.2 per cent, "other pulmonary diseases," with family history of epilepsy and insanity in 0.1 per cent of the cases and nervous diseases, syphilis, and other genitourinary diseases in about the same proportion.

In 69.7 per cent of the cases, no personal history of particular significance relative to disease conditions was reported. Nearly 20 per cent of the persons examined (19.4) were reported to have had rheumatism or gout, while 2 per cent (2.1) gave a history of typhoid fever. Six per cent (6.3) reported an old infection of gonorrhea and 0.5 per cent syphilis. Three per cent reported recent influenza; 0.5 per cent, ulcer of the stomach, intestines or other severe gastric disturbances; while 0.4 per cent of the cases reported each of the following: Tuberculosis, renal calculi, nervous breakdown, and neuritis. Three per cent had been operated upon for appendicitis and 2.1 per cent for hernia. The results of these family and personal histories are, we believe, of relatively little value.

4. **Conditions Most Frequently Observed.** It has been noted from the analysis of certain facts relative to personal hygiene that a large proportion of these people commit errors of diet, work too long hours, take too little exercise, and complain of fatigue. On the basis of a broad classification of defects found on examination, the proportion of advanced and serious defects is found to be highest at the older age groups, while minor and moderate defects are common among young men. It will be interesting to study the incidence of specific physical impairments in the broad age divisions. The chief findings, tabulated below, present an extraordinary picture of the large number and gravity of the impairments found in a group of persons who are up and about and apparently able to carry on their day's work. The findings themselves supply good reason for these examinations.

5. **Posture, Build and Weight.** An important factor in medical selection for life insurance is the applicant's build. A comparatively small percentage of these examined persons showed correct posture, and relatively few were of ideal weight for age and height. In this group, one-fifth (19.1 per cent) of the individuals were classed as having

TABLE II.—PERCENTAGE OF PERSONS IN SPECIFIED AGE GROUP SHOWING PHYSICAL IMPAIRMENTS.

16,662 white males in M. L. I. Company, Ordinary Department, 1921.

Impairment.	All ages.	Under 25.	25 to 34.	35 to 44.	45 to 54.	55 and over.
Persons in specified age group { Number	16,662	861	5885	5799	3023	1094
Persons in specified age group { Percentage	100.0	100.0	100.0	100.0	100.0	100.0
Build, posture and weight:						
Faulty posture	19.1	16.4	16.9	19.1	20.8	29.1
Spinal curvature	5.2	7.0	4.9	5.2	4.8	5.9
Flat feet	16.4	16.8	17.0	16.6	15.4	13.7
Over 20 per cent underweight	2.4	2.0	3.2	2.3	1.5	2.1
Over 20 per cent overweight	12.9	4.9	8.1	14.4	18.9	19.8
Eyes and ears:						
Defective vision corrected	25.4	15.2	18.4	21.8	38.3	48.7
Defective vision uncorrected	29.5	28.3	28.9	30.0	29.4	31.8
Otitis media; discharging ear	1.2	2.0	1.3	1.0	1.2	0.5
Nose and throat:						
Deflected septum, slight	22.8	24.5	24.5	23.0	19.9	19.2
Deflected septum, marked	2.7	2.6	2.8	3.1	2.4	1.4
Enlarged septic or buried tonsils	26.2	34.0	32.8	25.6	17.1	13.0
Nasopharyngitis, chronic	5.5	4.9	6.0	5.4	5.0	4.4
Nasopharyngitis, acute	5.5	6.5	5.5	5.5	5.0	6.2
Hypertrophic rhinitis, enlarged turbinates	14.8	19.0	16.9	15.1	10.7	10.1
Teeth and root infection:						
Carious teeth; septic roots	8.5	6.4	7.9	8.1	9.2	13.0
Slightly infected gums	10.3	3.6	7.3	11.1	14.7	16.4
Pyorrhea, definite	4.8	1.2	2.7	5.7	7.1	7.4
Heavy dentistry, roentgen ray advised	41.8	30.0	40.7	44.2	43.5	38.8
Heart and pulse:						
Functional murmur or irregularity	6.0	6.9	5.5	5.5	6.3	9.3
Mitral murmur, stenosis	0.2	0.2	0.2	0.1	0.2	0.4
Mitral murmur, regurgitation	0.7	0.3	0.7	0.5	0.9	1.5
Aortic murmur, stenosis	0.1	...	0.1	0.1	...	0.2
Aortic murmur, regurgitation	...	...	...	...	0.1	0.1
Enlargement	2.7	1.7	2.1	2.0	3.7	8.2
Slow pulse, below 58	1.4	1.4	1.0	1.4	1.7	1.9
Rapid pulse, above 90	8.3	10.9	8.2	8.2	8.6	6.7
Intermittent pulse, extrasystoles	0.5	0.2	0.4	0.4	0.8	1.7
Bloodvessels and blood pressure:						
Normal condition of bloodvessels	77.4	89.5	83.6	76.6	71.6	55.2
Slight arterial thickening	14.3	7.2	10.9	14.9	18.2	24.0
Moderate arterial thickening	4.6	2.0	3.1	3.9	6.5	13.6
Marked arterial thickening	0.6	0.1	0.4	0.3	0.7	3.7
Blood pressure, 15 to 25 below average:	9.9	7.6	7.9	10.9	12.1	10.2
Blood pressure, 25 or more below	2.4	0.6	1.3	2.9	3.3	4.3
Normal blood pressure	80.5	86.9	85.9	80.6	74.4	62.4
Blood pressure, 20 to 40 above average	6.2	4.6	4.6	4.9	8.3	16.4
Blood pressure, 40 to 60 above average	0.7	0.1	0.2	0.5	1.1	4.3
Blood pressure, 60 or more above average	0.3	0.1	...	0.1	0.7	2.3
Stomach; abdominal organs:						
Constipation	39.7	34.6	39.5	40.4	40.1	40.3
Tenderness over liver and gall bladder	0.6	0.1	0.4	0.8	0.9	0.7
Tenderness in region of appendix	2.3	1.7	2.5	2.5	2.1	1.6
Hemorrhoids	12.3	4.4	9.3	12.8	17.7	16.3
Abdominal organs; inguinal region:						
Weak inguinal rings	5.9	5.8	5.9	6.0	5.9	5.2
Inguinal hernia, no truss	2.2	1.4	1.4	2.2	3.1	4.8
Inguinal hernia, truss worn	2.9	0.2	1.4	2.6	5.1	8.2
Varicocele	8.1	9.9	8.5	7.8	7.8	6.9
Genitourinary:						
Prostate gland, enlarged, hard, tender or boggy	3.9	1.0	2.0	3.1	5.6	15.8
Endocrine disturbances:						
Enlarged thyroid; simple goiter	2.1	3.1	3.3	1.6	1.1	0.8
Miscellaneous impairments:						
Headache	15.4	13.7	16.4	16.6	13.7	10.0
Use of patent medicines	8.8	6.3	8.9	9.5	8.5	7.4
Use of laxatives	9.1	6.4	7.6	9.1	11.4	12.6
Frequent colds	17.7	22.9	20.8	16.4	14.2	13.6
Urinary findings:						
Normal	78.3	78.6	79.9	79.5	76.0	70.1
Albumin, slight trace	12.9	12.5	12.3	12.4	14.2	15.8
Albumin, definite trace	2.4	3.5	2.4	1.8	2.5	5.2
Albumin, marked amount	0.8	1.4	0.7	0.7	0.9	1.2
Sugar, trace	3.6	4.4	3.2	3.6	4.1	4.2
Sugar, marked amount (quantitative)	0.5	0.1	0.3	0.3	1.0	1.1
Casts, granular or epithelial	0.4	0.3	...	0.5	0.7	0.8
Casts, hyaline	4.1	4.2	3.0	4.0	5.3	7.5
Indican	3.9	3.1	4.0	4.0	3.7	4.4

definitely faulty posture, while more than one-eighth (12.9 per cent) were more than 20 per cent overweight.* As would be anticipated, both of these factors increase in magnitude with advancing age. Over 16 per cent of the men were reported to have flat feet, the age periods under forty-five having the highest proportion in this respect. Those who were more than 20 per cent overweight had a considerably higher proportion of flat feet cases at age periods of thirty-five and over than did men who were slightly overweight, underweight or of normal weight. The group of foot defects, it will be remembered, were stated to be by far the most numerous of all defects found in the population of military age.[1] Flat-foot cases amounted to approximately 12 per cent (301,146 cases) of the full military population considered.

Over 5 per cent of the cases of the present study showed spinal curvature which is considerably higher than that noted for the draft examinations, but the group in the latter instance consisted entirely of young men among whom this condition would naturally be less common.

6. **Overweight.** Overweight is a condition associated with various physical impairments. Obviously, the habits of life which are associated with this condition are also related to other physical defects. In this discussion, we shall deal primarily with the findings for persons more than 20 per cent overweight in relation to height, assuming the average for age thirty as standard for all later years, as based on the standard height and weight tables of the Medico-Actuarial Investigation of 1912.

The data were tabulated to show the number and percentage of persons in each age period who were of normal weight according to the standard table, and the number and percentage showing specified departures from the assumed norms. An abstract of the facts for persons 5 per cent under to 5 per cent overweight (the normal group) and 20 per cent or more overweight is shown in Table III.

The percentage of normal or average weights decreased from a maximum (31.7 of persons in the specified age period) at the youngest age interval fairly regularly with advancing age. The proportion of overweights (persons 20 per cent or more above average) was 4.9 per cent at the ages under twenty-five years, and increased with advancing age.

This rising ratio of overweight with advancing age furnishes a clue to the increasing incidence of defects of the cardiovascular-renal system with advancing age. These defects indicate not only the effect of senescence, but of increasing strain upon the circulatory and renal apparatus by reason of the accumulation of adipose tissue.

* Weight and height records were taken with the coat and vest removed and the shoes on. The applicant was then stripped to the waist for the examination of heart, lungs and abdomen, and further disrobing attained with the progress of the examination.

TABLE III.—NUMBER AND PROPORTION OF (*a*) TOTAL WHITE MALE ORDINARY POLICYHOLDERS, (*b*) THOSE 5 PER CENT UNDERWEIGHT TO 5 PER CENT OVERWEIGHT, AND (*c*) THOSE OVER 20 PER CENT OVERWEIGHT, IN SPECIFIED AGE DIVISIONS.

Age division, years.	Number of cases.			Percentage of total in weight class for each age division.		
	All cases.	5 per cent underweight to 5 per cent overweight.	Over 20 per cent overweight.	All cases.	5 per cent underweight to 5 per cent overweight.	Over 20 per cent overweight.
All ages	16,662	4295	2145	100.0	25.8	12.9
Under 25 . . .	861	273	42	100.0	31.7	4.9
25 to 34 . . .	5885	1607	479	100.0	27.3	8.1
35 to 44 . . .	5799	1456	836	100.0	25.1	14.4
45 to 54 . . .	3023	697	571	100.0	23.1	18.9
55 and over . .	1094	262	217	100.0	23.9	19.8

Among the overweights, 75 per cent (75.4) were classed as individuals having advanced or serious physical impairments requiring systematic, and in many cases, medical or surgical attention. Twenty per cent (19.6) of the overweights had moderate defects requiring medical supervision as well as hygienic correction. The normal weight group showed only 20 per cent with advanced or serious impairments, with 75.1 per cent showing moderate defects of varying degree.

The heart examinations showed no material difference between overweights and normals with respect to valve damage but there was a higher proportion of enlarged hearts (3.4 per cent) and pulse above 90 (10.9 per cent) among overweights than in persons of normal weight (2.5 and 7.1 per cent respectively).

The findings with respect to condition of the bloodvessels are of interest. Persons definitely overweight show smaller percentages of arterial thickening than do normals, and yet the proportion of persons with blood pressures 20 to 40 mm. of mercury above normal for age was 12.8 per cent among those who were overweight as compared with 5.2 per cent among normals. Whether or not this discrepancy between the proportion of persons with arterial thickening and of moderately high blood pressure may be due more to the difficulty of palpating the radial artery in stout persons than to any real difference in the actual arterial condition of persons is difficult to ascertain. While it has been believed in some circles that high blood pressure and arterial thickening necessarily go together, Allbutt,[2] and others have presented clinical and statistical evidence to show that they are not always associated. Allbutt also calls attention to the error of regarding arterial degeneration as a senile

disease rather than a condition or tissue change which may be due to many causes, especially infections in youth. Varicose veins were discovered in 5.7 per cent of the overweight cases and in 4.3 of those of normal weight. The proportion of cases of both normal and overweight individuals showing certain impairments of the bloodvessels is shown in the following table:

TABLE IV.—PERCENTAGE IN TOTAL OF EACH AGE GROUP OF NORMAL AND OVERWEIGHT PERSONS SHOWING SPECIFIED IMPAIRMENT OF BLOODVESSELS AND ABNORMALITIES OF BLOOD PRESSURE.

Impairments in weight classes.	All ages.	Under 25.	25 to 34.	35 to 44.	45 to 54.	55 and over.
OVERWEIGHT* GROUPS.						
Total overweights	100.0	100.0	100.0	100.0	100.0	100.0
Normal bloodvessels	79.2	97.6	87.1	80.6	75.8	61.3
Slight arterial thickening	14.1	..	8.4	15.0	16.3	20.7
Moderate arterial thickening	3.8	2.4	2.5	2.2	4.6	11.1
Marked arterial thickening	0.2	..	..	..	..	2.3
Varicose veins	5.7	..	2.1	4.7	8.2	12.0
Normal blood pressure	77.8	92.3	85.1	82.7	68.2	61.3
Blood pressure, 15 to 25 below	5.3	2.6	2.7	5.4	7.5	6.0
Blood pressure, 25 and more below	1.2	..	1.1	1.2	1.9	0.5
Blood pressure, 20 to 40 above	12.8	5.1	10.1	9.8	17.9	20.3
Blood pressure, 40 to 60 above	1.9	..	1.1	0.8	2.4	6.9
Blood pressure, 60 or more above	1.0	..	..	..	2.1	5.1
NORMAL WEIGHT GROUPS.						
Total normal weights	100.0	100.0	100.0	100.0	100.0	100.0
Normal bloodvessels	77.9	90.1	82.9	78.2	70.2	52.7
Slight arterial thickening	14.5	6.6	11.8	15.2	18.7	24.4
Moderate arterial thickening	4.6	2.6	2.9	3.8	7.3	14.5
Marked arterial thickening	0.6	..	0.2	0.1	1.0	4.6
Varicose veins	4.3	1.1	2.7	4.5	6.6	9.9
Normal blood pressure	81.7	86.6	87.7	81.1	73.8	62.7
Blood pressure, 15 to 25 below	10.1	7.1	7.0	11.8	14.9	9.8
Blood pressure, 25 or more below	2.2	0.7	0.8	3.1	3.0	4.3
Blood pressure, 20 to 40 above	5.2	5.6	4.3	3.4	6.8	17.3
Blood pressure, 40 to 60 above	0.6	..	0.2	0.5	1.0	3.9
Blood pressure, 60 or more above	0.2	..	..	0.1	0.4	2.0

* Over 20 per cent above standard.

This close relationship between high blood pressure and overweight is exceedingly significant, particularly at the middle-age periods. With regard to weight reduction in the management of hypertension, Rose[3] states that he has observed "an almost uniform and in the majority of cases, a satisfactory reduction of high blood pressure during the process of weight reduction through dietary control. Thereby the accompanying symptoms, notably shortness of breath, palpitation, edema of lower extremities, albuminuria

(due to congestion of the kidneys), headache, distention with gas, difficult locomotion and painful feet are quickly relieved."

Overweight and Blood Pressure. In the foregoing table we found that there was a higher percentage of hypertension cases (20 mm. Hg or more above average or normal blood pressure for age) among overweights than in persons of normal weight. Certain interesting details are set forth in Table V.

TABLE V.—PERCENTAGE OF PERSONS IN EACH AGE GROUP SHOWING SYSTOLIC BLOOD PRESSURE 20 MM. HG. OR MORE ABOVE AVERAGE OR NORMAL FOR AGE.

Age division.	Overweights (20 per cent or more overweight for height and age) (*a*)	Normal weights (5 per cent over or under average for height and age) (*b*)	Difference (*a*–*b*).	Odds in favor of inherent relation.*
All ages . .	15.7	6.1	+9.6	Practical certainty.
Under 25 . .	5.1	5.6	− 0.5	Sample inadequate.
25 to 34 . .	11.2	4.5	+ 6.7	Over 20,000.
35 to 44 . .	10.7	4.0	+ 6.7	Over 15,000,000.
45 to 54 . .	22.4	8.2	+14.2	Over 730,000,000.
55 and over .	32.0	23.1	+ 8.9	32.

* For method of calculating these odds see Pearl, Raymond: Medical Biometry and Statistics, Philadelphia, Saunders, 1923, p. 218.

Note: The numbers of persons included in the several age groups are shown in Table II.

At the youngest age group the number of cases was insufficient to warrant attaching any significance to the difference in the percentage of hypertension cases found in overweights and in normal weights. But for ages beyond 25 there was practical certainty that the differences between the percentage incidence of hypertension among overweights and those for normal weights are dependably significant of the effect of overweight.

Overweight and Urinalysis Findings. A somewhat lower proportion of normal urines (74 per cent) was found among overweights than among persons of normal weight (80 per cent). More of the overweight persons showed albumin (slight trace 14.3 per cent; normals, 12.4 per cent; definite trace, 3.8 per cent; normals, 2.1 per cent; marked amount 1.2 per cent; normals 0.5 per cent). The appearance of albumin in the urine becomes marked for overweights at the older age periods, and at ages of fifty-five and over we find that a definite trace or marked amount was noted in 12.2 per cent of the cases, as compared with 6.4 per cent for the normal weight group.

For age periods of thirty-five years and upward, sugar in the urine is considerably more common among overweight people than among

those of normal weight. The incidence of casts, (granular, epithelial and hyaline), is also noticeably greater among overweight persons. While no tests were made as to the significance of the differences in the percentages of urinary abnormalities found in overweights and in normal weights, it is clear from the findings for blood pressure that for the ages beyond twenty-five, the ratios are based upon dependable numbers, and that the differences in the percentages are significant of the effect of overweight. It is clear that overweight and dietary excesses tend not only to embarrass the circulatory apparatus, but that they also impair renal efficiency.

TABLE VI.—PERCENTAGE OF (*a*) NORMAL AND (*b*) OVERWEIGHT PERSONS SHOWING SPECIFIED URINARY IMPAIRMENT BY AGE GROUPS.

Impairments in weight classes.	All ages.	Under 25.	25 to 34.	35 to 44.	45 to 54.	55 and over.
OVERWEIGHT GROUP.						
Total overweights*	100.0	100.0	100.0	100.0	100.0	100.0
Normal urine	74.0	78.0	76.8	76.0	72.5	62.9
Albumin, slight trace	14.3	9.8	12.9	13.6	14.8	19.5
Albumin, definite trace	3.8	..	3.8	2.6	3.1	11.2
Albumin, marked amount	1.2	..	1.3	0.9	1.7	1.0
Sugar, trace	4.6	2.4	2.9	4.7	6.1	4.9
Sugar, marked amount	0.9	2.4	0.7	0.6	1.1	1.5
Pus	3.3	..	3.1	3.3	3.3	3.9
Casts, granular or epithelial	0.9	..	0.9	0.6	1.3	1.0
Casts, hyaline	6.3	4.9	4.9	5.3	7.2	10.7
Indican	3.4	2.4	2.9	4.0	2.6	4.9
NORMAL WEIGHT GROUP.						
Total normal weights	100.0	100.0	100.0	100.0	100.0	100.0
Normal urine	80.0	80.2	80.9	81.7	77.7	71.9
Albumin, slight trace	12.4	12.3	11.9	11.9	13.9	14.1
Albumin, definite trace	2.1	3.2	1.9	1.7	2.0	4.4
Albumin, marked amount	0.5	1.2	0.5	0.3	0.5	2.0
Sugar, trace	3.1	4.8	3.0	2.5	3.5	3.6
Sugar, marked amount	0.5	..	0.4	0.2	0.6	2.4
Pus	2.8	1.6	2.5	2.5	3.5	4.8
Casts, granular or epithelial	0.4	..	0.2	0.3	0.9	0.8
Casts, hyaline	3.5	4.0	2.2	3.3	5.1	6.8
Indican	3.6	1.6	4.2	3.4	3.6	2.8

* 20 per cent or more above standard.

It follows, therefore, that the detection of overweight in early life and the correction of this defect through dietary and other hygienic counsel, would materially reduce the number of persons in the general population having hypertension. This would consequently postpone serious embarrassment of the circulatory appara-

tus and would eventually affect favorably the number of cardiac and renal involvements which today follow in the train of excessive alimentation.

7. **Circulatory System.** Physical examination revealed conditions abnormal in some degree with respect to heart and pulse in 17.2 per cent of the cases. Examiners were urged to give special consideration to cases of overrapidity or adventitious sound that might be due to nervous excitement. Functional murmur or irregularity occurred in 6 per cent, organic murmur in 1 per cent, heart enlargement in 2.7 per cent and rapid pulse (above 90) in 8.3 per cent, with slow pulse (below 58) in 1.4 per cent of those examined. These cases of heart murmur and enlargement, as might be expected, are notably more frequent among the older age groups. Slow pulse, likewise, is more common at the older ages and among low blood pressure groups. Rapid pulse, on the other hand, is higher among groups manifesting high blood pressure, and also among men under twenty-five years of age.

Abnormalities of the bloodvessels, of varying degrees, were noted in 22.6 per cent of the cases. Arterial thickening was recorded in 19.5 per cent of the cases, but only to a slight degree in 14.3 per cent. Clinical and experimental evidence[4, 5, 6], indicates that arterial disease, when associated with hypertension is the result rather than the cause of hypertension. Varicose veins were noted in 4.6 per cent of the cases.

Blood Pressure. The question of blood pressure in relation to overweight has already been discussed. Certain aspects of the problem of blood pressure, however, are worthy of special consideration here in view of the interest in this subject on the part of commissions, life insurance groups and public health workers. It may be stated at the outset that the blood pressure readings were usually taken with mercurial instruments, and by the auscultatory method. The life insurance standards of average blood pressure for age used by the Life Extension Institute were determined by analyses of many thousands of cases and were checked by extensive investigations in independent centers. Only 80 per cent of the policyholders included in the present study were found to have normal blood pressure according to the standards used.*

On account of the manner in which the original data were classified it is impossible to submit records of average blood pressures

*. While there is still some difference of opinion concerning the relation of the factor of blood pressure to the condition of the vessels, it may be noted that high arterial pressure is believed by Barr to be the primary cause of degenerative changes in the arteries, but once these changes are established we get a vicious cycle, as they increase the work of the heart, and thus maintain the high pressure. The walls of the vessels may also be directly affected by toxins and microörganisms, such as the spirocheta pallida and the typhoid bacillus (Sir James Barr: High Arterial Blood Pressure: Its Nature, Causes, Effects and Treatment, Am. Med., 1923, **18**, 349)

for different age periods. For our purposes, however, it is chiefly essential to determine by use of accepted standards clear departures from the normal. One of the most instructive studies of healthy men and women is that of Symonds.[7] This report included 150,419 men entrants who were risks accepted by the Mutual Life Insurance Company of New York for the years 1907 to 1919 inclusive. His findings indicate that the blood pressure of healthy men of age period fifteen to nineteen, taking the average of all builds is 123.5 systolic, and at the ages of sixty and over it is 135.2 systolic.

Clinical and pathologic observations on hypertension indicate a lack of unanimity as to its etiology and pathology.[8] Symonds states that the mortality ratios do not definitely prove that a systolic pressure of 140 mm. in the years below forty is of pathological significance, but for pressures above 145 mm. they indicate it strongly. Hunter[9] recently called attention to the fact that persons with distinctly high pressure are prone to develop diseases of the heart, blood vessels and kidneys, the mortality from heart disease, apoplexy, and Bright's disease being very high among them. In many instances, at least, Moschcowitz[10] says the pathological changes in the kidney of Bright's disease are the results rather than the cause of hypertension. Other investigators have approached the problem from the point of view of anthropometry and biophysics, emphasizing items such as vital capacity, growth type, viscosity of the blood, peripheral resistance, and so forth.

Stocks,[11] in an extensive statistical study, insists that from twenty to forty years of age systolic blood pressure below 98 mm. should be considered to be pathological, and below 109 mm. to be suspicious. Diastolic blood pressure does not reach its maximum at the same time as does the systolic pressure, but usually when adolescence is passed.

The data here presented relate to 13,308 cases of normal systolic blood pressure, or cases of blood pressure not departing either way from the limits of 20 mm. above or 15 mm. below the life insurance standard for the given age. In comparison with these figures there is an analysis of 1021 cases showing blood pressure ranging from 20 to 40 mm. above the average for age. The standards used for the various ages appear in Appendix Table A and have been previously reported,[12] as has the following table, taken from Dr. Fisk's original paper, but reprinted here as a background for further discussion.

These data are exceedingly interesting and, in certain cases, somewhat surprising. Literature has emphasized the importance of such items as overweight, high protein diet, the excessive use of tobacco, the existence of focal infection of the tonsils and in the dental structures. All of these, either singly or in combination, have, at times, been associated with the existence of abnormal blood

pressure,* either high or low. From these records, however, it appears that of the various factors mentioned, overweight is the outstanding one consistently accompanied by a markedly higher percentage of high blood pressure, although the condition of "heavy dentistry" also shows higher ratios.

TABLE VII.—A STUDY OF 1021 CASES OF HIGH BLOOD PRESSURE AND RELATED IMPAIRMENTS AND LIVING HABITS COMPARED WITH 13,308 CASES OF NORMAL BLOOD PRESSURE.

Physical defects and influential living habits.	Normal blood pressure, 13,308 white males (20 mm. above to 15 mm. below the standard). Per cent all ages.	High blood pressure, 1021 white males (20 to 40 mm. above standard for age). Per cent all ages.	High blood-pressure cases as compared to normal (+ or −). Differences.*
High protein diet	38.4	38.5	+ 0.1
Excess of tea and coffee	40.8	44.3	+ 3.5
Alcohol, moderate	6.9	8.8	+ 1.9
Alcohol, excess	0.6	1.1	+ 0.5
Tobacco, temperate	12.1	13.8	+ 1.7
Tobacco, excess	33.1	31.0	− 2.1
Functional heart signs	5.6	9.6	+ 4.0
Valvular defects	0.8	2.4	+ 1.6
Hypertrophy	2.2	7.8	+ 5.6
Myocardial changes	0.1	1.0	+ 0.9
Rapid pulse (90 and over)	7.7	18.7	+11.0
Arterial changes	17.8	35.2	+17.4
Tonsils, defective	26.5	26.9	+ 0.4
Caries of teeth	8.1	9.7	+ 1.6
Recession and pyorrhea	14.4	19.4	+ 5.0
Heavy dentistry, roentgen ray advised	41.4	42.7	+ 1.3
Insufficient dentistry	5.4	7.2	+ 1.8
Gastric, acid stomach, etc.	17.8	17.9	+ 0.1
Constipation	39.2	38.4	− 0.8
Albuminuria	14.7	18.1	+ 3.4
Casts	3.9	6.6	+ 2.7
Pyuria (marked or persistent)	2.7	3.5	+ 0.8
Glycosuria	3.8	5.0	+ 1.2
Overweight, 10 to 15 per cent	9.3	11.0	+ 1.7
Overweight, 15 to 20 per cent	7.5	9.5	+ 2.0
Overweight, over 20 per cent	12.6	25.5	+12.9

* No tests of the significance of these differences have been made.

Blood Pressure and Diet. Among males in this series who partook of too high protein diet,† the proportion of hypertension cases present

* While investigators agree that the immediate cause of hypertension is unknown, it has been shown by Moschcowitz and others that among the remote causes, psychic factors play an important role. The importance of peripheral resistance, congenital or otherwise, in the causation of hypertension has also been indicated. (Moschcowitz, E.: Congenital Peripheral Resistance: Its Causative Relation to the Precocious Hypertensive States, Arch. Int. Med., 1924, **33**, 566.)

† For the purpose of this classification, high protein diet is one in which meat or other concentrated protein food is taken in liberal quantities two or more times daily.

in each group is practically identical (7.3 per cent for "too high protein diet" and 7.4 per cent for all other persons). This observation is in line with previous findings by several other workers.[13] At each of the age divisions no important differences in the percentages of hypertension cases were found as between "high protein" feeders and "all other" white males (see Table VIII). While there is some evidence that high protein diet, excess of epinephrin in the circulation and disturbances in sodium chlorid metabolism may be concerned in the production of high blood pressure, it is interesting to note that Strouse[14] and Mosenthal[15] found high protein diets to be without effect on the blood pressure of hypertensive cases, that Mosenthal[16] states that no definite proof of a relationship of the suprarenal glands to high blood pressure has been produced, and that O'Hare and Walker[17] believe that salt plays little or no role in the etiology of arterial hypertension.

TABLE VIII.—BLOOD-PRESSURE READINGS ON CASES (*a*) SHOWING AND (*b*) NOT SHOWING SPECIFIED IMPAIRMENT. 16,662‡ WHITE MALES, ORDINARY DEPARTMENT. 1921.

Impairment.	Total cases.		Percentage of total in impairment group with					
	No.	Per cent.	Normal blood pressure.	Blood pressure, 15 to 25 below average.	Blood pressure, 25 or more below average.	Blood pressure, 20 to 40 above average.	Blood pressure, 40 to 60 above average.	Blood pressure, 60 or more above average.
Weight:								
20 per cent or more overweight	2,033	100.0	77.8	5.3	1.2	12.8	1.9	1.0
Normal weight*	4,251	100.0	81.7	10.1	2.2	5.2	0.6	0.2
Diet:								
Too high protein diet	6,253	100.0	81.7	8.9	2.1	6.3	0.7	0.3
Residue†	10,105	100.0	79.3	10.7	2.6	6.2	0.8	0.4
Use of tobacco:								
Excessive use of tobacco	5,466	100.0	80.6	10.4	2.4	5.8	0.5	0.3
Residue†	10,892	100.0	80.0	9.8	2.4	6.5	0.9	0.4

* Five per cent above or below average weight for age and height.
† All others not showing specified impairment.
‡ In 304 cases, blood pressure or other readings were not taken.

Blood Pressure and the Use of Tobacco. While the figures applying to tobacco users may not be conclusive, it may be noted here again that the difference in blood pressure classification between those who are listed as "temperate" and "excessive" users and as

nonusers is only slight. Temperate users are those who smoke less than 4 cigars or 9 cigarettes or 9 pipefuls daily. These observations correspond with those reported by Hunter[18] in which it was stated that a moderate use of tobacco does not seem to have much influence on the blood pressure. Another check is available through the analysis of some 5520 cases of excessive tobacco users in the life extension groups,[19] among whom there was no excess ratio of high blood pressure cases, although other important impairments were found such as increased ratio of arterial thickening, mouth infection, and those showing rapid pulse.

A convenient consolidation of blood pressure data for groups (*a*) showing a specified impairment and (*b*) not showing the impairment is shown in Table VIII.

Low Blood Pressure. The findings with respect to low blood pressure indicate that overweight persons, high protein eaters, had relatively fewer individuals with low blood pressure than did the normal control groups. Low blood pressure was only slightly, perhaps insignificantly, pronounced among excessive users of tobacco (see Table VIII).

8. **Respiratory System.** The chief interest attached to the records obtained from examination of the lungs and other respiratory organs is in the fact that 97.2 per cent were reported normal. Less than ½ of 1 per cent of the cases (0.4) showed suspected or incipient tuberculosis, while only 6 cases were found to have the disease in advanced or moderately advanced form. Sputum examinations were not made in routine. A little over 1 per cent of the cases (1.2) had acute or chronic bronchitis and 0.4 per cent, asthma.

Conditions of the upper respiratory tract showed more striking deviations from the normal. Twenty-five per cent (25.5) showed deflected septum and 26.2 per cent enlarged, septic or buried tonsils. Only 7 cases were reported to have adenoids. Enlarged turbinates were found in 14.8 per cent of the cases.

9. **Digestive System.** Fifty-five per cent of the men examined showed teeth defects, 8.5 per cent of them with carious teeth, 10.3 per cent with slightly infected gums and 4.8 per cent with definite pyorrhea. These conditions were considerably higher, as might be expected, at the older age periods. As previously noted, 41.8 per cent of the cases showed that considerable dental work had been done. The data were not adequate, however, to warrant detailed analysis at each age period.

Fifty-four per cent of the individuals had some form of stomach or abdominal conditions. Constipation was reported in 39.7 per cent of the cases. This condition has been suspected of being a factor in the causation of high blood pressure, but our figures do not show any relationship in this respect. "Acid stomach" is reported in 9.8 per cent and gastric disturbances in 8.2 per cent of the cases.

Observations of tenderness in the region of the appendix (2.3 per cent), weak inguinal rings (5.9 per cent) and inguinal hernia (5.1 per cent), are of interest, as these findings are not frequently reported in collections of medical statistics.

10. **Genito-urinary System.** The urinalysis findings in 78.3 per cent of the cases were negative, while a slight trace of albumin was found in 12.9 per cent and a definite trace or marked amount in 2.4 per cent of the cases. Sugar was present in 3.6 per cent of the cases (marked amount, by quantitative methods in 1.5 per cent of the cases). The association between overweight and albumin and sugar in urine has been previously mentioned. Somewhat similar relationships are noted between these urinalyses findings with respect to overweight classes and those related to high blood pressure groups, although the entire significance of these findings is entirely clear. In Table VI it is noted that the proportion of cases showing albuminuria, casts and glycosuria is much higher for the high blood pressure given than among men having normal blood pressure. Evidence is accumulating[20] that renal and vascular lesions may be the result of hypertension rather than the cause, although until recently, hypertension was considered entirely the result of arterial and renal disease. Hyaline casts were found in 4.1 per cent of the cases and granular or epithelial casts in 0.4 per cent, and pus in 2.9 per cent. These conditions are considerably more abundant at the later age periods.

Previous history of gonorrhea was reported in 6.3 per cent of the cases. In 23.4 per cent of these cases, rheumatism or gout was reported, as compared with 19.4 per cent in the total group studied. In this group of cases, the presence of heart murmurs and heart enlargement is higher, and, as might be expected, albumin and pus in urine are more frequently discovered than in cases without such history.

11. **Nervous System.** There is little of interest to report relative to brain and nervous conditions as found by these examinations except that abnormalities of various grades of seriousness were reported in 16 per cent of the cases, nervousness ranking highest and sluggish or absent reflex, second.

Defective vision was reported in 54.9 per cent of the cases, with corrections in 25.4 per cent. Defective hearing was reported in 15.4 per cent of the cases and otitis media, or discharging ears, in 1.2 per cent.

12. **Endocrine System.** Endocrine disturbances were found in 2.3 per cent of the cases; 2.1 per cent showing enlarged thyroids.

13. **Miscellaneous Findings.** Chronic skin infections, such as acne, dermatitis, eczema and others, were reported in 10.4 per cent of the cases and frequent headache, in 15.4 per cent. Nearly 9 per cent (8.8) of the individuals reported the use of patent medicines. Frequent colds were mentioned in 17.7 per cent of the total cases studied.

APPENDIX A.—STANDARD OR NORM SYSTOLIC PRESSURES (MM. HG.) AT VARIOUS AGES.

Age.	Millimeters.	Age.	Millimeters.
15 to 20	120	41 to 45	129
21 to 25	123	46 to 50	131
26 to 30	124	51 to 55	132
31 to 35	124	56 to 60	135
36 to 40	127		

14. **Conclusions and Recommendations.** It is entirely credible that the facts shown for this group of more than 16,000 males are indicative of conditions in the general population of white males. If so, it is clear that a wider extension of periodical health examinations among the adult population is indicated. Hygienic advice and the prompt treatment of both the major and minor defects thus discovered may lead to the prevention of serious consequences to these individuals later on. Most of the defects and impairments discovered in the younger ages of adult life are subject to effective control.

Perhaps the most helpful prospect is in the field of weight control. These figures show conclusively that marked overweight is associated with serious impairment of cardiovascular function, and this suggests that recognition and control of excess body weight may lead to a sharp reduction in the actual number of individuals with embarrassed hearts and bloodvessels.

The facts on hygienic habit are unique. No other data of similar scope are available in the literature. The statement of the facts under this heading ought to stimulate the extension of hygienic instruction.

Since this is a first study, too much should not be expected from the cross relationships of the data. For certain states which give premonition of serious ill-health in later life, we need more observations in order that conclusive evidence may become available for refined study. The facts on focal infection in relation to systemic disorders should be sharpened. This may be possible in physical examinations to be made in the future. The present study suggests that where we have at present mere traces of important connection between premonitory conditions and the later and graver disabling disorders, we may in the future be able to collect data which establish definite relationships.

The next important step for preventive medicine is to secure facts which will firmly establish the effective control of diseases of the heart, bloodvessels and of the renal tract. Preventive medicine will be confronted not only with the early discovery and the prompt treatment of premonitory states, but with the problem of critically testing the several methods available for the prevention of serious physical breakdown in middle and later life. It is quite possible that careful tests of the several procedures available will show which of these offers maximum results for effort expended.

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REVIEWS.

BACTERIAL INFECTION. By J. L. T. APPLETON, JR., B.S., D.D.S., Professor of Microbiology and Bacteriopathology, the Thomas W. Evans Museum and Dental Institute, School of Dentistry, University of Pennsylvania. Pp. 474; 91 engravings and 5 colored plates. Philadelphia and New York: Lea & Febiger, 1925. Price, $6.00.

THE purpose of the author is to provide a textbook of bacteriology, with special reference to dental practice. In Part I are presented fundamentals of bacteriology—morphology and physiology of bacteria; disinfection, sterilization and classification. Both the older nomenclature appearing in classifications of Migula and of Chester, and the recent nomenclature and classification of Bergey are given. Part II deals with the nature and types of infection; with factors predisposing to infection; with natural, humeral and cellular defenses of the host against bacterial invasion; and with immunity. Part III is of value particularly to the dentist. It includes a discussion of special infections of the oral cavity and presents methods for clinical dental bacteriology.

The book fulfills its object—"to present an adequate conception of infection and a comprehensive understanding of the bearing of infection on the problems of dental practice." W. K.

INDUSTRIAL POISONS IN THE UNITED STATES. By ALICE HAMILTON, A.M., M.D., Assistant Professor of Industrial Medicine, Harvard Medical School; Formerly Special Investigator of Poisonous Industries for the United States Bureau of Labor Statistics. Pp. 590. New York: The Macmillan Company, 1925.

THIS is an excellent and very valuable book. It brings its rapidly moving subject up to date and will entirely supplant the authoritative works of a decade ago. The book is carefully compiled and written, and the presence of numerous references adds to its value.

It is interesting to note that in spite of all the increase in industrial chemical processes almost two-fifths (two hundred pages) of

the volume are devoted to lead poisoning. This will probably not long be true of such works. In the present instance it represents partly the special interest of the author and her colleagues in Boston in this topic.

The author has omitted all consideration of industrial health hazards not strictly due to chemical poisons. Thus the harmful effects of dust *per se* is not discussed, although one might feel that the title, *Industrial Poisons*, would be broad enough to include pneumokoniosis from silica. The book is by no means a complete review of occupational diseases, but is a very important contribution to the chemical phases of this subject. P.

MORTALITY STATISTICS (1922). TWENTY-THIRD ANNUAL REPORT. Department of Commerce, Bureau of the Census. Washington: Government Printing Office, 1925. Price, $1.90.

AMERICAN ILLUSTRATED MEDICAL DICTIONARY (DORLAND). Edited by W. A. NEWMAN DORLAND, M.D. Thirteenth edition. Pp. 1344; 338 illustrations. Philadelphia and London: W. B. Saunders Company, 1925. Price, $7.00.

THE great activity of medical science is so frequently adding new words to its vocabulary that new editions of medical dictionaries are frequently desirable. In this edition "about 2500 new words make their first appearance." I wonder how many have been dropped from the twelfth edition. Since the first edition in 1900 there have been forty-one reprints and new editions of this popular book. E. K.

THE CONQUEST OF CANCER. By H. W. S. WRIGHT, M.S., F.R.C.S. Pp. 82. New York: E. P. Dutton & Co., 1925. Price, $1.00.

THIS booklet is one of the "Today and Tomorrow" series which has produced the well-known *Dædalus*, *Icarus*, *Tantalus* and others. It aims to present in popular manner what may be accomplished by better coöperation between the public and the medical profession toward the conquest of cancer. Believing that "the quest for a single causal factor whose 'discovery' will lead us to 'abolish cancer' is just one more hunt for the philosopher's stone" and the theory that "right living" is the best insurance against cancer today, the author tells us in plain terms what the individual should do toward insuring himself. Without accepting some of his theo-

retical dicta about the genesis of cancer, we can heartily endorse the never-too-frequently-to-be repeated principle that the public must be educated to seek expert diagnosis and treatment at the earliest possible moment. Unfortunately it must also be added that it is still necessary to educate some of the profession in the same principles.

The introduction by F. G. Crookshank, which by the way occupies one-third of the book, contains a general statement about malignant disease and a short disquisition on "the" cause of disease which could be read with profit by medical investigators in general as well as by those for whom it is here intended. E. K.

THE INTERNATIONAL MEDICAL ANNUAL. A Year Book of Treatment and Practitioner's Index. Forty-third year. Pp. 548; 43 plates and 87 illustrations. New York: William Wood & Co., 1925.

APART from the criticism applicable to year books in general, the overemphasis placed upon the new, radical and evanescent, there is little but approbation which can be said for the forty-third issue of the *Medical Annual*. It gives an excellent summary of the progress of the year in medicine and surgery as interpreted by a staff of twenty-eight contributors, many of whom are men of international eminence. The alphabetical arrangement of the subjects is a helpful feature of this work which will appeal to the practitioner, as will also the emphasis which is placed upon treatment. A.

GOITER: NONSURGICAL TYPES AND TREATMENT. By ISRAEL BRAM, M.D., Instructor in Clinical Medicine, Jefferson Medical College, Philadelphia. Pp. 479; 152 illustrations. New York: The Macmillan Company, 1924.

A PRESENTATION of thyroid disease by a man who does not believe in the surgical treatment of exophthalmic goiter, but prefers rest and medical measures. So far, so good; but the extremeness of the author's views, a prolix, rambling style with endless repetition, and not a few statements scientifically inaccurate hopelessly outbalance some good clinical observations. Surgery is dismissed with "to say the least, the prognosis of Graves' disease under surgical treatment is hardly better than if the patient were left alone to take his chances with spontaneous recovery." Of questionable, unproven or erroneous propositions are such: That "leukopenia is to be regarded as pathognomonic of Graves'

disease;" that a flesh diet is potent stimulation to endocrine dysfunction, causes goiter and therefore a meat-free diet is imperative in *simple* goiter; that "ordinarily the ingestion of 100 gm. of sugar causes no increase in the normal individual's blood (sugar). . . . In hyperthyroidism this quantity increases the normal content to about double;" that the basal metabolism is routinely increased in diabetes mellitus. Again under the section of the treatment of Graves' disease are advised: Pancreatic extract by mouth for glycosuria; ichthyol for the cardiac symptoms; routine injection of horse serum before parturition to prevent bleeding; while quinin, the author's favorite drug, is said to counteract the excess of iodin in the blood; electrotherapy is much extolled. R. K.

MEDICAL AND SURGICAL REPORT OF THE ROOSEVELT HOSPITAL, NEW YORK. Pp. 378; 47 illustrations. New York: Paul B. Hoeber, 1925.

AFTER a lapse of ten years the second *Medical and Surgical Report of the Roosevelt Hospital* now makes its appearance. In addition to reprints of articles which have appeared in various medical and surgical journals, the *Report* contains articles which have been written expressly for this work. The names of Dowd, Dwight, Floyd and Peck are attached to sixteen of the thirty-four papers. J. A.

A TEXT-BOOK OF GENERAL BACTERIOLOGY. By EDWIN O. JORDAN, PH.D., Professor of Bacteriology in the University of Chicago and in Rush Medical College. Eighth Edition, thoroughly revised. Pp. 752; 179 illustrations. Philadelphia and London: W. B. Saunders Company, 1924.

IT is pleasing to note the biennial regularity with which new editions of this excellent text-book of general bacteriology appear. Years of use as a text for teaching have added refinement and perfection of presentation through seven careful revisions.

The present eighth edition contains new material on the bacteriophage phenomenon, tularemia, botulism, scarlet fever, and other subjects in which recent progress has been made. J. S.

PROGRESS

OF

MEDICAL SCIENCE

MEDICINE

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Parenchymal Rales in Pulmonary Tuberculosis: Their Clinical Significance.—One of the most puzzling and difficult problems of physical diagnosis is the proper interpretation of the rather small moist rale, elicited by coughing, heard over the chest of the normal individual at times, but most frequently over some area of pulmonary tissue that may be the seat of an active lesion or the location of a preëxisting process now inactive, or rather incapable of producing symptoms. As BRUNS (*Jour. Am. Med. Assn.*, 1925, **85**, 739) remarks, rales of this type are generally accepted as important signs of chronic parenchymatous tuberculous lesions. Furthermore, these rales are usually considered to be the result of moisture in the terminal bronchioles. That such is not the case, the author attempts to show by a process of clinical deduction and by a study of lungs removed at autopsy. Both methods of study are open to serious objections, particularly the latter method of removing the lungs, inflating them with bellows, observing where rales are heard through the auscultory stethoscope and then sectioning this area for evidence of moisture, pneumonia, congestion or tubercle. Gross evidence of disease would be observed, but the method is not sufficiently refined to determine the presence or absence of moisture in the smaller bronchioles or alveoli. Therefore it cannot be proven by this method that these so-called indeterminate rales are produced by the sudden opening of collapsed lobules and that moisture is not present in the alveoli. The author's contention that these rales are atelectatic in origin is a belief that is held by many internists, and despite the criticism of his method of proving

his case, the procedure he employs is probably as accurate as any devised up to the present. That portion of the paper which deals with the author's clinical cases seems to the reviewer to contain the real meat of his presentation. He calls forcible attention to the fact that indeterminate rales may exist for years in individuals who are apparently in every other respect normal and buttresses his arguments with 5 well-selected cases. The author will have performed a real service if he is able to correct the very general misconception of the genesis of rales of this character and can impress upon the physician the fact that such rales do not necessarily mean tubercle without confirmatory proof from the history, symptoms, laboratory and roentgen-ray examination.

Plague: Past, Present and Future.—The most interesting observations made by LLOYD (*Jour. Am. Med. Assn.*, 1925, **85**, 729) have to do with the laboratory diagnosis and the treatment of plague. He speaks from an experience, which incidentally must have been appalling, which includes the management of 1491 cases occurring in Guayaquil, Ecuador, during a period of two years. In order to make a bacteriologic diagnosis of plague from postmortem tissue, the author recommends the following procedures: Inoculate 3 guinea pigs, 1 intraperitoneally, 1 subcutaneously and the third by rubbing the infected material on the clipped unbroken skin of the abdomen with the flat side of a dull knife. This latter method is the best in order to procure a pure culture of the Bacillus pestis. The growth is subsequently transferred to a moderately dry agar slant and to bouillon, where it presents certain typical characteristics. In the treatment of plague only one method merits serious consideration—the use of fresh antiplague serum in doses of 80 to 100 cc. initially, with succeeding doses of 40 cc. every twelve hours until all danger is passed. The author writes that he is mindful of the fact that antiplague serum is looked upon with great skepticism by many prominent men in the United States, but he expresses himself unequivocally in favor of this method of treatment, provided that fresh serum is given early in the course of the disease in large doses.

The Prognostic Value of Differentiating Immature Neutrophils in the Blood.—This very short paper is of interest because it recalls to our mind the necessity of making a careful morphologic study of the white cells, when making a differential count of the leukocytes in those conditions in which the microscopist is usually expected simply to report upon the percentage of polymorphonuclears present in the blood smear. DE COURCY and THUSS (*Ohio State Med. Jour.*, 1925, **21**, 487) detail the blood counts in 10 cases of sepsis, and show that the presence of immature forms of neutrophils in a ratio greater than 3 or 4 per cent is of decidedly bad prognostic import, and that the higher the percentage of the young forms rises the more serious is the prognosis. They use Schilling's classification of young cells: (1) Cells smaller than myelocytes, with a single deeper staining nucleus than in the myelocyte, round and often slightly indented; (2) staff-shaped single nucleus staining deep, deeply indented in shape of horseshoe and often having the appearance of the letter S.

The Vital Capacity of the Lungs in Relation to Clinical Medicine.—ARNETT (*Boston Med. and Surg. Jour.*, 1925, **193**, 157) gives an excellent review of the present-day knowledge of the vital capacity of the lungs. He brings out one point which properly could bear repetition and accentuation: Routine determination of the vital capacity of the person in good health should be advised because if this is known, and as there is no known standard except that of the individual, variations from this standard will be of value in determining early cardiac and pulmonary disease.

Cases Illustrating the Indications for the Use of Quinidin Sulphate in Heart Disorders.—WHITE and SPRAGUE (*Boston Med. and Surg. Jour.*, 1925, **193**, 91) present a clinical paper with a report of 15 cases of heart disease treated by quinidin sulphate in order to illustrate the type of case in which quinidin is of value and the type in which it is valueless, or even harmful. The authors point out that so much has been written concerning the dangers of the drug that medical men have become most timorous in making use of a drug that has a very real worth. To illustrate their point they quote in detail 2 cases of paroxysmal auricular fibrillation, 1 case of paroxysmal tachycardia and 5 cases of resistant auricular fibrillation. The 7 cases in which quinidin was valueless include 1 in which the drug was given in large amounts without proper supervision of the patient, 2 in which the indications were doubtful, 1 in which there was extensive heart disease, 1 other in which there was congestion failure and, lastly, 1 of those rare cases in which the drug caused the patient to have marked evidences of cinchonism. The three most important contraindications to the drug are a history of congestive failure, extensive heart disease and sensitiveness to the drug.

SURGERY

UNDER THE CHARGE OF

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Massive Excision of Subcutaneous Abdominal Fat. — HEINECK (*Virginia Med. Month.*, 1925, **52**, 106) states that in suitably selected cases the operative removal from the abdominal wall of large, wedge masses of subcutaneous fat has the following advantages. It is a safe and invariably beneficial surgical procedure. (It has always been performed under general anesthesia.) It is always devoid of immediate or remote dangers to the patient. Although the wound is extensive, the hemorrhage is moderate and healing is good. It is simple

of execution, and if unassociated with another operative procedure the technic is easy and the performance of the operation does not consume much time. It is all important that the incisions be carried to but not beyond the fascia. It is not infrequently employed in conjunction with other operations. It eliminates a physical handicap, effects a marked improvement in the patient's appearance and general well-being and procures complete relief from an unsightly painful and disabling deformity.

Roentgenoscopic Evidence of the Association of Ureteral Stricture and Urinary Calculus.—HUNNER (*Jour. Urol.*, 1925, **13**, 497) says that the presence of a calculus in a kidney or ureter is presumptive evidence of a coëxistent ureteral stricture. Ureteral stricture is probably of blood-borne origin. It is practically always bilateral. The symptoms and many of the pathologic changes which were formerly ascribed to the presence of a stone are probably more often the result of stasis due to the stricture. Such phenomena as silent stone, renorenal reflex, calculous anuria with a stone obstructing on one side only, the frequent recurrence of stone on the side operated upon, the frequent postoperative development of stone on the opposite side, the recurrence of symptoms soon after operation—all can be explained in a more logical way. Many stones are silent, but the accompanying ureteral stricture is not often without symptoms. Reflex anuria, heretofore considered a nervous phenomenon, will likewise be found in most instances to be due to bilateral stricture and to depend on actual physical changes in the narrowed areas of both ureters.

The etiology of urinary calculus formation has been discussed in which the evidence for and against such theories as the chemical, microbic and the mechanical or urinary stasis theories have been set forth. No single theory is all-sufficient for the explanation of such a complicated problem as that of calculus formation. If, however, ureteral stricture can be demonstrated in approximately 100 per cent of the cases with stone in the kidney or ureter, it is evident that a new angle from the etiologic point may be taken.

Spastic Obstruction to the Ureters.—HEPBURN (*Ann. Surg.*, 1925, **81**, 1133) states that he is surprised that so little consideration has been given to the possible influence of the circular muscle rings found in the walls of the drain pipes of the urinary system. Physiologically the ureters conduct the urine from the renal pyramids by a peristaltic action similar to that of the alimentary tract. This contraction is seemingly independent of content and nerve supply. The first observation bearing on this hypothesis is that obstructions to the ureter are most commonly found at the following places: The ureteropelvic junction, at the point where the ureter goes over the iliac vessels, in the broad ligament portion in females and in the intramural or trigonal portion. Every one of these places is the location of a circular muscle band. The commonest point of obstruction is in the intramural portion. Not only is this group of circular fibers largest here, but they here practically become a part of the trigone and the two ureteral openings are connected by the interureteric muscle band. The diagnosis of ureteral obstruction due to interureteric muscle spasm is made

from history, the cystoscopic appearance of the interureteric muscle and from the ureterograms. Cutting the interureteric muscle and closing the cut anteroposteriorly in conjunction with dilatation of the intramural portion of the ureters with bougies is the best treatment for those cases that will not yield to hygiene or dilatation with bougies.

The Surgery of Hypertrophic Pyloric Stenosis.—ZIEROLD (*Minnesota Med.*, 1925, **8**, 393) says that it is probable that complete closure of the lumen rarely, if ever, occurs and that some portion of the feedings passes onward into the intestine, the resulting stool being more scanty than normal. This finding of persistently small bile-stained mucous stools is of the greatest significance, as it at once gives information as to the location and the severity of the lesion. Continued vomiting, accompanied by visible gastric peristalsis and starvation stools, implies failure of the stomach to empty, and if not promptly and effectively relieved by other means, is an indication for surgery. Gastroenterostomy, the operation of choice up to 1911, has been definitely discarded as unphysiological and dangerous. Today the generally accepted procedure is that of Rammstedt, either in its original form or as modified by Strauss. The fate of the tumor has been the subject of numerous investigations, of which Wollstein's are the most complete. In a histologic study of the pylorus in 25 infants, who died at various times, following operation, she found that a regular involution of the muscle occurs. Sixteen months after operation only a faint line is seen, and at two years the scar is scarcely visible.

Skeletal Traction.—MOORHEAD (*Am. Jour. Surg.*, 1925, **39**, 113) claims that skeletal traction has demonstrated itself as a useful and safe procedure in certain recent fractures, particularly that group in which reduction and maintenance has hitherto demanded open correction with or without the use of nonabsorbable material, such as plates, wires, screws, bands or clamps. Certain fractures of the femur, notably the supracondylar group are in many cases irreducible, except by open operation or skeletal traction. The latter is preferable, because it is safer and simpler. This procedure of skeletal traction has wide application in compound fractures, because the traction medium can be introduced at a distance from the wound and further because the necessary dressings can be unhampered, inasmuch as splintage is reduced to the minimum. The limb can be readily inspected and the method lends itself to mobilization of the entire musculature and adjacent joints. Skeletal traction with osteotomy through the fracture line replaces extensive operations in malunion and is a welcome substitute for bone reshaping or bone sacrifice, with or without metallic suturing.

The Surgical Treatment of Cancer of the Breast—JUDD (*Am. Jour. Roentgenol. and Rad. Therap.*, 1925, **13**, 411) believes that good results from surgical treatment of cancer of the breast depend more on early operation than on extensive procedures. Some of the early cases start with a high degree of malignancy and will recur in spite of early and radical treatment, while some of the fairly advanced cases, because they are of a lower degree of malignancy, will be cured by operation.

Cancer probably originates in a single focus; the avenues of its extension from the mammary gland are well understood. A radical operation in which the adjacent fascia, muscles and lymphatics are removed is essential in all operable malignant cases. But in spite of this procedure there will be early recurrences in certain apparently favorable cases. On the other hand, many patients in whom the disease is obviously extensive will remain well. In estimating the result of treatment for cancer of the breast it is obviously necessary to take into consideration the type and grade of malignancy dealt with. In a series of cases in which the malignancy is of low grade the results are sure to be better than in one composed almost entirely of highly malignant cases. There is very good evidence of the beneficial effect of radiotherapy alone in certain cases, including those in which recurrences have followed surgery, but there is every reason to believe that some combination of surgery and radiotherapy can be found which will do more than either alone.

Gonorrhea of the Epididymis.—GRANT (*Urol. and Cutan. Rev.*, 1925, **29**, 285) states that the treatment of epididymitis itself is a surgical procedure. Where the gonococcus has invaded the epididymis the most important factor consists in killing the gonococcus. The therapeusis of epididymitis is not a simple matter. It is almost impossible to reach this structure through the posterior urethra and ejaculatory ducts by the injection of drugs in solution. It is questionable whether any good is accomplished when the vas deferens is opened surgically for injection of some germicidal drugs. It has seemed that the gonococcus is an organism which is destroyed particularly easily by the application of heat. For example, if heat can be applied in such a way as to reach the gonococcus at a temperature of 112° F. for five minutes' exposure it is practically certain that the organism will be destroyed. The author has adopted the method advocated by Corbus of Chicago. The principle is to force heat into the epididymis itself at 106° to 108° F., continuing the application for thirty to forty minutes, which practically destroys all gonococci present. In order to do this two electrodes must be used through which the electric current passes and the heat accumulates in the center between these two electrodes. This method was used in a series of 35 cases of gonorrheal epididymitis. Only 1 patient failed to respond as promptly as is the rule. In this case there was a hydrocele of long duration. After it was tapped and heat applied to the epididymis a second time the patient was completely relieved.

Some Problems in Anorectal Surgery.—ZOBEL (*Am. Jour. Surg.*, 1925, **39**, 119) claims that individuals suffering from rectal trouble usually come to the surgeon complaining of one of the following symptoms: Pain, bleeding, itching or protrusion. Complaint may also be made of constipation, diarrhea or of a discharge of pus or mucus. In the majority of cases pain is found to be due to an anal fissure. In many of these sufferers, added to their pain, is the conscious or subconscious fear that the trouble may be a rectal cancer. As a matter of fact it may be safely stated that when there is severe pain in the anorectal region one rarely finds a cancer. As a rule, there is pain with

hemorrhoids only when they are eroded and inflamed or are thrombotic. A complete fistula causes little if any pain, except when its external opening closes. It is then practically an abscess. The author thinks that good judgment must be exhibited before an operation for the extirpation of a rectal cancer is advised. The patient's age, physical condition, circumstances and environment, the situation and duration of the growth, among other things, must be taken into account. In patients over sixty years of age, with a growth present for sometime, colostomy is advised, followed by massive roentgen-ray doses. The author has not drawn his final conclusions as to the value of the latter. In those under this age an extirpation of the growth should be attempted if there be even a fair chance for a good result. The two- stage or three-stage operations, with preliminary colostomy, give the best results as regards mortality. The use of radium is not advised.

Management of Intracranial Injuries with or without Fracture.—CONNORS (*Ann. Surg.*, 1925, **81**, 901) states that no case of intracranial injury should be operated upon until definite localization of the brain injury has been determined. If an operation is to be performed it should expose the brain laceration, remove the compressing substance and control hemorrhage. The subtemporal decompression operation as a routine measure fails in the majority of cases, because it does not expose the lacerated brain, remove the compressing substance or check the hemorrhage. In view of the fact that such an operation has not yet been demonstrated, palliative treatment is recommended in cases of *contre-coup* laceration of the brain.

Gastric Ulcer and Gastric Carcinoma: An Inquiry into Their Relationship.—DIBLE (*Brit. Jour. Surg.*, 1925, **12**, 666) says that his study shows that gastric ulcers coming to operation as such prove on their removal to be simple in nature almost invariably, and that gastric carcinomata, as far as can be judged by histologic evidence, are in a large majority of cases malignant from their inception. This is not a denial of the possibility of malignant change supervening in a chronic gastric ulcer. It is a conservative view of the frequency of this event. Experimental work in a variety of fields has clearly shown the tendency for a supervention of malignant diseases in sites of constant irritation of a certain grade. Malignancy may supervene in a chronic ulcer of any type, but apart from the continued applications of certain known irritants, it is not a common event. It may be conceded that a gastric ulcer, by virtue of its chronicity and constant exposure to the gastric juice, is more likely to be prone to malignant change than a simple ulcer in another situation. This is conceded, but it does not affect the conclusion that this change is not a common one. Gastric carcinomata occur most frequently closely to the pylorus. They may occur in the ulcer site, but it is not their commonest position. The history of gastric ulcer is long, while that of carcinoma is short. This diagnostic fact, so much emphasized by past generations, seems almost ignored by some of the modern schools. In the author's cases the average length of the history in the 108 cases of chronic ulcer, proved histologically in which this information was available, was ten years and four months, whereas the average length of history in the 28 simi-

larly proved cases of carcinoma was only two years and three months. The average age of his cases of ulcer and carcinoma at the time of operation is forty-four and forty-nine years respectively. When the duration of symptoms in the two conditions is taken into account the average ages of onset are found to be more widely separated, being thirty-three and forty-five years respectively.

THERAPEUTICS

UNDER THE CHARGE OF

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The Cure of Cardiac Fibrillation.—WENCKEBACH (*Therap. d. Gegen.*, 1925, **5**, 199) calls attention to the fact that there is no unanimity or opinion regarding the use of quinidin in cardiac fibrillation in spite of the large amount of work which has been done on this subject, and reviews the indications and contraindications for its use. He emphasizes the fact that quinidin is a cardiac depressant, and its action is antagonistic to the action of digitalis. On this paralyzing action rests the therapeutic use of quinidin in cases of cardiac extrasystole, tachycardia, flutter and fibrillation. In treating cardiac disease with this drug one must constantly remember these fundamental facts, and refrain from using it on patients with severe heart disease and extensive myocarditis. In his experience the author has found that it is useless and often harmful in those cases where by the use of digitalis therapy there is no improvement in cardiac action or circulation. In such cases the auricular fibrillation is responsible for only a small part of the circulatory disturbance, and to give the patient a drug which has a depressing action on the heart muscle should be avoided. The patients who have severe valvular disease, and particularly those with mitral stenosis and auricular fibrillation, should be given quinidin with great care. Because of the dilatation of the left auricle in these cases, and the stagnation of blood in this cavity, thrombi frequently form in the left auricular appendage. When the cardiac action becomes regular embolism may result from mobilization of these thrombi. Such a possibility does not contraindicate the use of quinidin in these cases, but a roentgen-ray will show marked dilatation of the left auricle and inform the physician if such a possibility must be considered. The chief indication for quinidin therapy is in treating those patients whose health and circulation are upset by the complete cardiac irregularity and whose heart muscle is in comparatively good condition. In such cases good results can be expected, for the fibrillation of the auricle is the main cause of the symptoms. It is important to watch the blood pressure when giving quinidin, for it lowers arterial tone, and should not be used in large doses on patients with low blood pressure. Cases of exophthalmic goiter can tolerate large doses of quinidin, and the

effect is to reduce the general overactivity of all bodily functions. It is useless to force or continue quinidin with those patients whose fibrillation returns after a few days or a week. Adaptation of the circulation to sudden or frequent changes of cardiac rate is hard for the patient, and it is better to regulate ventricular action by administration of digitalis. Before giving quinidin to cure auricular fibrillation, the patient should be put to bed and a test dose given of 0.25 gm., to find out if the patient has an idiosyncrasy to quinidin. If this amount is well tolerated the patient is given from 0.25 to 0.4 gm. four times a day. Occasionally normal heart rhythm is established in twenty-four hours; usually the cure lasts longer, even as long as ten days. Personal observation of the patient is essential, and if there is a marked fall in blood pressure, or if the patient complains of weakness, this treatment should be discontinued. In cases with dyspnea or signs of stasis from cardiac insufficiency a digitalis course should precede the quinidin course. To those patients whose hearts show only a slowing of rate and diminution of the arrhythmia after a course of quinidin one should give a course of digitalis therapy. When the ventricular rate has reached 70 or 80 beats a minute digitalis should be discontinued, and quinidin then will aid greatly in the treatment. There is no contraindication to the use of quinidin with digitalis in an attempt to effect ventricular action without attempting to cure auricular fibrillation. On the contrary, the older practitioners combined quinin and digitalis, and it was observed that patients so treated could tolerate larger doses of digitalis. Doubtless quinin in this respect is a welcome addition to our methods for reëstablishing a normal heart action.

Luminal in the Treatment of Epilepsy.—OSTMANN (*Deutsch. med. Wchnschr.*, 1925, **15**, 605) advocates the use of luminal in the treatment of epilepsy, and has avoided harmful effects from the use of this drug by withholding it from patients with high blood pressure and striking vasomotor disturbances. New cases he treats with 0.05 gm. of luminal given three times a day, and increases the dose by 0.05 gm. until attacks are under control. When this has been accomplished the successful dose is continued for four weeks and then gradually reduced by the same amount. Should epileptic symptoms appear again this dose must be increased until they are kept under control. Institutional cases were treated with the same object in view and the dose which was successful in controlling attacks was continued for ten days and then gradually reduced. When symptoms appeared the dose was gradually increased to the amount which controlled them and continued for ten days, when the smallest amount which controlled attack was determined. This was continued for a month. Usually this class of patients required 0.2 to 0.3 gm. of luminal a day, which was divided into three doses. Never was more than 0.6 gm. a day given. If results were not obtained with luminal alone it was combined with bromid. Luminal is not a specific drug in the treatment of epilepsy, but many cases were relieved, and of 30 cases treated by the author 28 were benefited, and 12 of these cases were able to work as long as they took the luminal.

Treatment of Vascular Filariasis.—TANON (*Presse méd.*, 1925, **17**, 265) has employed the arsenical preparation hectin for fourteen years in the treatment of filariasis, and reports not only amelioration of symptoms but permanent cures. In all cases where the embryos were present in the blood before treatment they quickly disappeared and the subjective symptoms gradually subsided. The majority of cases even after returning to the tropics had no relapse or return of filariasis. The technic consists of the subcutaneous or intramuscular injection of 0.2 gm. of hectin every other day for twenty days in cases which show at least one embryo in a microscopic field, and 0.1 gm. if less are found. A second series of ten injections is given after an interval of twenty days, using 0.1 gm. at each injection, given twice a week whether embryos are present in the blood or not. In the cases with elephantiasis general treatment has little or no effect on the local lesion, and massage and elastic compression is advised. Hectin has the advantage over other arsenicals which have been used in the treatment of filariasis, in that it is harmless. The author reports that he has never seen ocular disturbances or toxic manifestations from its use.

A Method for the Immediate Treatment of Salvarsan Infiltration.—DIETEL (*München. med. Wchnschr.*, 1925, **55**, 128) has found that the pain can be quickly controlled, and the infiltration caused by subcutaneously injected salvarsan relieved by immediate injection of 10 cc. of sterile physiologic saline solution. Aspiration alone of the salvarsan solution does not relieve the pain caused by the solution, and often there results an extensive inflammatory reaction. When necessary he aspirates as much of the salvarsan solution as possible, and immediately injects at the site of infiltration 10 cc. of sterile saline solution which not only dilutes the salvarsan solution in the tissues so that inflammation does not result, but the larger amount of sodium chlorid solution causes a more rapid withdrawal of the infiltrated salvarsan.

The Action of the Intravenous Injection of a Solution of 40 Per Cent Urotropin.—Since VOGT (*Zentralbl. f. Gynäk.*, 1921, **45**, 49) first advocated the intravenous injection of an aqueous solution of urotropin for the treatment of urinary retention this treatment appears to be the method of choice. RITSCHEL (*Deutsch. med. Wchnschr.*, 1925, **19**, 776) used this method in the treatment of 69 patients with urinary retention, and reports success in 94 per cent of cases. This method was used to give relief to patients suffering with postoperative retention, and also to relieve retention which occurred several days after operation, which was of nervous origin. The usual procedure was to inject 5 cc. of a sterile aqueous solution of urotropin on the evening after operation if necessary, and if no relief followed to repeat the same dose in an hour and a half to two hours. If catheterization was then necessary the danger of infecting the bladder was minimized. Sterile solutions of urotropin are prepared by the firm of E. Schering, and sold in ampules containing 5 cc. This solution must be injected intravenously for subcutaneous infiltration is followed by painful local inflammation.

PEDIATRICS

UNDER THE CHARGE OF

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Insulin in the Treatment of Malnourished Infants. — TISDALL, BROWN, DRAKE and CODY (*Am. Jour. Dis. Child.*, 1925, **30**, 10) studied the effect of the administration of insulin to malnourished infants. Nine infants received insulin in conjunction with the intravenous injection of 20 per cent glucose. Seven infants over a total of thirteen periods received insulin in conjunction with 15 per cent of glucose subcutaneously. Two infants received insulin in conjunction with 10 per cent glucose subcutaneously and 6 infants in conjunction with the feeding. A definite increase in the weight was obtained in 50 per cent of the cases. In these cases in many instances two factors were present which lessened the probability that insulin was the cause of the increase in weight. The intravenous injection of 20 per cent glucose and insulin together is probably not the most efficient method of administration. Insulin apparently produced the most marked diminution in the elevation of the blood sugar when administered about one and one-half hours before the glucose. The effect of the insulin on the blood-sugar concentration varies tremendously in different infants, consequently its administration is not without danger. Certain infants may have a very marked hypoglycemia without showing any hypoglycemic reaction. No positive evidence was obtained that insulin of itself, when administered with carbohydrate to undernourished children produces any beneficial effect.

Anemia in a Newborn Infant.—SANFORD (*Am. Jour. Dis. Child.*, 1925, **30**, 19) reports a case in which there was a marked anemia in an apparently healthy newborn infant at birth. The blood showed evidence of extreme activity, such as high white cell count and nucleated red blood cells, with poikilocytosis and polychromasia, and decreased blood-platelet formation. There was no evidence that there was an increase in blood destruction, for the jaundice which appeared on the second day and disappeared on the fourth occurred during the improvement of the blood picture and normal bleeding and coagulation time. The van den Bergh test for hepatic bilirubin was positive, suggesting this jaundice was of hepatic origin. During this time the liver also decreased in size. The spleen steadily decreased in size as the blood picture improved, and this occurred without treatment of any kind, unless the roentgenogram of the extremities was in some sense a factor. The increase in hemoglobin continued more rapidly than the increase in erythrocytes, and the color index was kept over rather than under 1. It was known that the mother's blood picture was normal at the time of this delivery, and also that the older brother's blood was normal. There was no family history of syphilis, tuberculosis, debility or mis-

carriages. The factor of a maternal influence must, therefore, be ruled out. No explanation of the before-mentioned condition can be offered. The child's recovery was rapid and complete without treatment in any way—except for the slight exposure to the roentgen ray.

Gastric Analyses in Normal Infants and in Those Convalescent from Diarrhea.—DAVISON (*Am. Jour. Dis. Child.*, 1925, **30**, 23) states that the presence of swallowed saliva or of regurgitated duodenal material is an important factor in reducing the gastric acidity of normal infants and of those convalescent from diarrhea, and also in determining to some extent the types of organisms found in gastric contents. Less than one-third of the specimens of gastric contents of these infants were free from salivary or duodenal contamination. Diets of some form of lactic acid milk increased the gastric acidity, but there was very little evidence that either these diets or the increased gastric acidity resulting therefrom destroyed many organisms in the stomach. The acidity of specimens collected less than six hours after a meal was higher than that of specimens collected later. This difference may have been due to the fact that all of the specimens collected later than six hours after a meal contained saliva. Elevation of the body temperature decreased the gastric acidity but this change can possibly be explained by the frequency with which the gastric contents of febrile infants was contaminated with saliva. The presence of vomiting increased the gastric acidity. Practically no difference could be found in the reaction or cultures of the gastric contents of normal infants and of those convalescent from diarrhea. As reported in a previous contribution the author found that the more acid the gastric contents, the greater the acidity of the duodenal contents obtained less than one-half hour later. The reaction of the gastric contents did not have any apparent relation to the amounts of duodenal amylase and trypsin. This observation does not agree with the usual physiological conception that the acidity of the gastric contents stimulates the flow of pancreatic juice, bile and intestinal secretions. Duodenal cultures were more frequently sterile in infants whose gastric acidity was from pH 5.1 to 5.7 than in those in whom it was from pH 3.6 to 4.4. No observations were made on the relationship of the psychic state of the infant and the results of the gastric analyses, but it is possible that any form of excitement may affect the gastric secretion. All of these factors should be taken into consideration before conclusions in regard to the gastric secretion can be drawn from analyses of gastric contents in infants.

Tuberculosis in Children.—DROLET (*Am. Rev. Tuberc.*, 1925, **11**, 292) reveals that during the last twenty-six years in New York City 28,762 deaths from various forms of tuberculosis have been reported among children under fifteen years of age. In 1898, 1370 such deaths were reported among a total childhood population estimated at 1,002,767. In 1923, with a child population increased by more than 675,000, the tuberculosis death rate was reduced to only 547. The former death rate of 136 per 100,000 was reduced to 33, or by 76 per cent. In children under fifteen years of age tuberculosis meningitis causes one-half of the deaths. The death rate from this cause in

children in New York City has been reduced from 78 to 17 per 100,000, or by 78 per cent, between 1898 and 1913. In this group of children pulmonary tuberculosis is the next important type after the meningeal form, and nearly one-third of all of the tuberculosis deaths among children were of this form. The death rate which was 31 per 100,000 was reduced to 10, or by 68 per cent. Pulmonary tuberculosis, though it has greatly decreased in New York, has not been reduced quite as fast as the other forms. The abdominal type of tuberculosis in children under fifteen years of age in New York City, though causing a large proportion of the deaths, showed the greatest decline. Until recently the death rate from tuberculous peritonitis frequently reached 7 and 8 per 100,000, whereas in the last couple of years it has gone down to 1 per 100,000. The causes of these declines are attributed to the measures that the health authorities have adopted. The first is the complete pasteurization of milk, except the certified, and the second is the annual examination of almost 100,000 food handlers, as the belief is that the greatest part of the transmission is by means of contaminated food supplies.

The Diagnosis of Tuberculosis in Childhood.—SMITH (*Atlantic Med. Jour.*, 1925, **28**, 725) states that the most common and most positive finding in children who have positive tuberculin reactions is the presence of small rounded shadows outside of the hilus. These have been shown by autopsy to be small tuberculous foci in the lung or along the bronchi. They may be very faint if the tubercles are young, denser if fibrosed and very dense if calcified. They may be very few just outside of the hilus, or may be scattered throughout the lung in small numbers, or may be numerous. These small mottled shadows are not seen when the tuberculin reaction is negative. They are nearly always present when the tracheal whisper is transmitted lower than the fourth dorsal spine. It is not claimed that the presence of these small foci is responsible for the increased whisper transmission, but they are probably like sentinels, showing that there are greater changes in the mediastinum due to lymph nodes or lung involvement. Pleural thickenings, especially interlobar plastic pleurisy or effusions, always suggest tuberculosis. Infiltrations of the lung tissue with many small or large shadows are seen in disseminated or bronchopneumonic tuberculosis and in general miliary tuberculosis. The lung involvement often starts from the hilus region. A true caseous pneumonia casts an even shadow, involving a part of or all of a lobe. It rarely has the distribution of a lobar pneumonia. Fibrosis, cavitation and all of the later changes are seen in older children. From these statements it is evident that in a child tuberculosis in the bronchial nodes is the most frequent lesion found, and is at the same time very easily overlooked. Like many other obscure conditions in medicine, one has to think of its presence in order to make the diagnosis. When a child is seen who is pale and droopy, distinctly undernourished, or with a history of loss of weight, with bright eyes, long lashes and hairy arms and nape, tuberculosis should be suspected. A positive tuberculin test will show that the child harbors the bacillus. Then a temperature record should be kept to see if there is activity of the process. A careful physical examination, with special attention to the intrascapular region, will

often show a tracheal whisper to the fifth or sixth dorsal spine, and occasionally an asymmetrical upper line of pulmonary resonance. The lungs should also be examined with great care, especially in the nipple region and axilla, for persistent dry rales here are suggestive, as are signs of dry pleurisy or effusion. The superficial nodes must all be palpated, and the abdomen carefully searched for masses or ascites. The spine and bones must be carefully examined. Signs of early meningitis, such as crossness, headache and vomiting, must not be forgotten. The roentgen-ray plate may show definite lesions, but even when it is quite normal we are justified in localizing the disease in the bronchial nodes in the absence of other definite findings. The only signs may be a positive skin test, the aspect of the child, a failure to gain weight, a slight irregular fever, a lowered transmission of tracheal whisper and a few small dense shadows outside of the hilus. This makes a symptom complex which is definite enough, once the evidence is all put together. Such children need care, and need it at once, before the trouble extends to vital organs. They do wonderfully under a proper regime, but may do badly if neglected. A few weeks or months of rest cure, with sun, air and proper food, will often bring the temperature down to normal, start a rapid gain in weight and change the entire appearance of the child, as well as its future progress. Still it is a sad fact that many such children are up and about, driven to school or to play, when the evidence is quite plain on their faces to one with seeing eyes. The hope of stamping out this plague lies in attacking it here in its truly incipient stage, while the results are apt to be good, instead of waiting for the serious and almost hopeless later stages to develop. All physicians should learn to be on the alert for these early curable cases.

Vaccine and Serum Treatment in Bronchopneumonia of Children.—DUFOURT (*Presse méd.*, 1925, **33**, 829) studied 100 cases of bronchopneumonia, and he showed that the disease is usually caused by the pneumococcus, enterococcus and sometimes by both. The streptococcus was found in 1 or 2 out of 10 cases, and almost was in secondary bronchopneumonia. He used a vaccine containing the pneumococcus, enterococcus, staphylococcus and the tetragenus. The vaccine was used alone in 80 per cent of all the cases. A dose of 0.25 or 0.5 cc. was injected on the first day in infants and young children. On the second day 0.33 or 0.5 cc was given and on the third day 0.5 to 1 cc. were given. Daily injections of 1 cc. were continued until fever and grave functional signs subsided. In older children and in adults a double dose was given. An improvement of local and general phenomena occurred after three or four injections. If five or six vaccine injections failed then antistreptococcic serum was tried in a dose of 30 cc. in infants and 60 cc. in children. In bronchopneumonia caused by streptococci improvement under the serum appeared on the third day. The injection of the serum was continued daily until definite disappearance of the infection.

DERMATOLOGY AND SYPHILIS

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Intravenous Bromid Therapy in Eczema.—Lebedjew had reported in 1924 the beneficial effect observed in the treatment of acute vesicular eczema, especially when a neurotic factor was involved through the intravenous injection of sodium bromid. Since the original report several additional favorable reports have appeared, including the present one by HUBSCHMANN (*Dermatol. Wchnschr.*, 1925, **80**, 828). The method seems to be effective in proportion to the acuteness of the process. Itching and oozing may disappear from an acute extensive eczema almost overnight. In the more chronic cases relief is slower, but the majority of patients are helped. Chronic eczema shows the least response. The drug is injected intravenously in doses of 10 cc. of a 10 per cent solution of sodium bromid in physiologic salt solution. Initial doses of 3 to 5 cc. may be given but are rarely necessary. Two to five injections are often sufficient, but as high as fifteen may be necessary to give relief.

Chronic Erythema of the Legs in Young Women Due to Thin Stockings.—WEBER (*Brit. Jour. Dermatol. and Syph.*, 1925, **37**, 259) discusses in a very interesting fashion the recent contributions to the literature and his own observations on a chronic erythema of the leg in the region of the ankle, occurring in young girls and associated with sclerodermatous thickening and nonpitting elephantiasic changes in the affected skin. While the condition at its outset suggests to some extent erythema induratum of Bazin, all observers are agreed that apart from a hypostatic background, it has no connection with the tuberculous condition. Apparently there is a permanent atony of the superficial blood capillaries. In some cases there seems to be an assotion of chilblain-like lesions. MacCormac, Dore and the author himself feel satisfied that the wearing of thin silk stockings and short skirts in cold weather is the exciting cause acting upon a predisposing skin and vascular background.

Treatment of Skin Sensitization to Sunlight by Peptone Injections.—CASTLE (*Brit. Jour. Dermatol. and Syph.*, 1925, **37**, 267) reports a case of an elderly man, who for fifteen years had suffered from extreme irritability of the skin on exposure to sunlight. Four injections of Martindale's peptone and a quinin cream apparently produced a com-

plete cure. The fourth injection was followed by a fairly severe reaction but without unfavorable effect. The patient was able to return to South Africa, from which country he had been an exile on account of his condition.

Purpura Hemorrhagica and the Treatment of Syphilis.—Very few reports of the complication of arsphenamin treatment, long known in Europe as aleukemia hemorrhagica, have appeared in American literature. The condition is apparently an unfamiliar one. Inasmuch as it is a grave complication of neoarsphenamin and sulpharsphenamin treatment, it deserves greater notice. O'LEARY and CONNER (*Am. Jour. Syph.*, 1925, **9**, 262) report 2 cases following the administration of sulpharsphenamin, in both of which they were able to ascertain that the rapid destruction of blood platelets and the lengthening of the bleeding time were the two most striking features. The leukopenia which has formerly been regarded as connecting the condition with aplastic anemia did not occur in one of their cases and was not extremely pronounced in the other. There was moreover some increase in the large mononuclear count. The first patient apparently recovered as a result of subcutaneous injection of 1 cc. of fibrogen. The second patient received 1 cc. of a 3 per cent solution of coagulen ciba subcutaneously and 0.75 gm. of sodium thiosulphate intravenously. The authors feel that hematopoietic crises may have been responsible instead of medication for both recoveries. The bleeding times and platelet counts were not markedly affected by this treatment. It is interesting to note that LASERSOHN (*Jour. Am. Med. Assn.*, 1925, **85**, 436) reports a case of so-called "hemorrhagic encephalitis" following sulpharasphenamin injection, in which the clinical picture of multiple cutaneous hemorrhages with hemorrhage into the subdural space and blood in the spinal fluid is much more suggestive of a syndrome of postarsphenamin hemorrhagic purpura with coincident cerebral hemorrhage than it is of the typical hemorrhagic encephalitis. This case was treated with sodium thiosulphate without result.

Nonspecificity of the Luetin Test.—SMITH and GILL (*Am. Jour. Syph.*, 1925, **9**, 292), using a commercial preparation, found that the luetin tests with the material which they employed were completely nonspecific and unreliable in diagnosis.

Sensitization to Adhesive Plaster.—BROWN (*Arch. Dermatol. and Syph.*, 1925, **12**, 69) reports a second case in the literature of specific sensitivity to a particular adhesive plaster. No effort was made to investigate the element in the composition of the adhesive plaster responsible for the sharply defined local dermatitis which it produced, but the fact that the particular brand of adhesive plaster was responsible was apparently established beyond discussion.

Etiologic Factors in Erythematous Lupus.—THRONE (*Arch. Dermatol. and Syph.*, 1925, **12**, 33) studied 38 cases, reaching the conclusion that in early cases of the discoid type removal of focal infections before atrophy sets in, together with simple local treatment, is apparently curative. Removal of focal infections seems to prevent recurrences.

Vaccine treatment (using a hemolytic streptococcus vaccine) was of no value. No evidence of a tuberculous factor in the condition could be discovered. On the contrary, a tuberculous cause in discoid erythematous lupus seemed to the author to be eliminated.

Influence of Potassium Iodid on Experimental Syphilis in the Rabbit.—PEARCE (*Arch. Dermatol. and Syph.*, 1925, **12**, 1) apparently demonstrated that the regular administration of small bi-weekly or weekly doses of potassium iodid to rabbits (0.006 and 0.0003 gm. per kilogram) modified the severity and shortened the duration of the experimental disease as measured both by the character of the primary orchitis and the general manifestations. The disease which developed in the rabbits treated with iodid resembles in many ways that of normal rabbits of relatively high resistance in which few or no secondary lesions arise. It is suggested that the therapeutic action of potassium iodid in experimental syphilis of the rabbit is associated with the stimulation or reinforcement of the host's resistance mechanism.

The Wassermann Test, with Special Reference to Sulpharsphenamin.—BELDING (*Arch. Dermatol. and Syph.*, 1925, **11**, 736) finds that prolonged treatment with the arsphenamins may not give as favorable serologic results as varied or mixed treatment. From his cases it appeared that sulpharsphenamin does not offer a sufficient difference from other arsphenamins to make it a valuable aid in treating arsphenamin-fast patients with fixed positive Wassermann reactions.

GYNECOLOGY

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Actinotherapy of Genital Tuberculosis. — According to SCHMITZ (*Radiology*, 1925, **4**, 283), actinic therapy is rapidly gaining in importance in the treatment of surgical tuberculosis, and therefore a report of his observations on the treatment of tuberculosis of the female genitourinary organs with ultraviolet light and roentgen rays may be of practical value. The technic employed in his clinic consists in the daily application of a light bath of an hour's duration from an Edison carbon light diffused by a reflector. The anterior and posterior body surfaces are each exposed for one-half hour. This is followed by the application of the ultraviolet light obtained from an air-cooled quartz light, according to Rollier's method. The head is always covered and the body is divided into five parts. The exposures begin with one

minute anteriorly and posteriorly on the first day, and are gradually lengthened until exposures of fifteen minutes are used daily over anterior and posterior surfaces. With this method erythema is never seen, but a pronounced tanning of the skin is produced. The treatment is given every other day as soon as the local findings begin to improve and twice a week for an entire year when local healing has been attained. If a rise in temperature should occur the treatment is interrupted until the patient has been afebrile for ten days. If the tuberculous exudate or infiltrate does not begin to decrease within four to six weeks roentgenotherapy is added to the violet-ray treatment. The roentgen rays are applied locally, and they must be hard and filtered to produce a homogeneous penetration of the entire diseased area. The dose must be small and should be from 10 to 5 per cent of a full skin dose attained at the depth of the disease. The 5 per cent dose may be repeated every three weeks, and the 10 per cent dose every six weeks until resolution of the tuberculous process is complete, which occurs ordinarily within four to six months. If after the second roentgen-ray treatment the general and local condition has not markedly improved then the case may be considered refractory to actinic therapy. The roentgen rays may also cause a temporary amenorrhea, which is desirable. Actinic therapy does not interfere with surgical procedures that might be indicated as the evacuation of abscesses or the removal of ascitic fluid through a celiotomy. The ascitic fluid should always be removed if it has been present longer than four weeks. There must also be no neglect of the general management, as absolute rest in bed, open air, sunshine, wholesome nourishing food and medication.

Roentgenotherapy of Uterine Cancer. — A report from Leningrad, based on 421 cases treated by radium between the years 1914 and 1921, has been presented by POLUBINSKY (*Zentralbl. f. Gynäk.*, 1925, **49**, 1193). Of this group there were 309 cases of primary carcinoma of the uterus, 13 cases of malignant disease of other organs, 4 benign tumors of the uterus, 39 recurrences after radical operation for uterine cancer and 56 cases in which prophylactic irradiation was given after removal of the uterus. In this clinic 25 to 30 mg. of radium element is used for twenty-four hours, repeated every three to four days until ten to thirteen treatments are given, or a total dosage of from 7000 to 8000 mg. hours. The mortality of the series was 4 per cent, chiefly from sepsis, while complications, such as inflammatory exudate, pus collections and hemorrhage occurred in 7.8 per cent and fistulas occurred in 9 per cent of the cases. Satisfactory primary results were obtained in 91 per cent of the cases, while an average of 20 per cent of all cases showed a good late result. In general the recurrent cases reacted poorly to irradiation. In the cases that were irradiated after radical operation there was only a 2 per cent mortality, and there were only 14 per cent of recurrences. The end results were poor in the cases of cancer of the vagina, vulva, ovary and rectum. As a result of ten years' experience the author believes that in cervical cancer radium gives just as good results as operation and without mortality nearly as great. This is especially noted in cases where the cancer has already begun to pass into the borderline stage of operability. If the cases have been subjected to radical operation it is always advisable to

give prophylactic irradiation. It should be remembered that the application of radium is dangerous and of no value in cases that are cachectic, in the presence of metastatic tumors, in cases where the tumor is adherent to the pelvic bones and in the presence of fistula. The results of radium irradiation are dependent upon the age of the patient (worse in young women), the extent of the disease, the histologic structure of the tumor (the results are poorer in cylindrical-cell carcinoma than in flat cell growths) and on the size of the dose.

Ovarian Dermoids.—As the result of his analytical study of the histories of 100 consecutive patients with ovarian dermoids who were treated in the Mayo Clinic, KOUCKY (*Ann. Surg.*, 1925, **81**, 821) states that the presence of the ovarian dermoid is not markedly inimical to conception and childbearing. In this series 20 women had never been married. Sixty (75 per cent) of the 80 married patients had borne a total of 184 children. Three of the remaining 20 patients had had miscarriages, leaving 17 of the married women who had never been pregnant. Of these, 3 had been married two years or less, 9 had large uterine fibromata, while in 5 the dermoid cyst was the only gross pathologic condition and may have been a cause of the sterility. Forty-two patients came to the Clinic with no complaint referable to the dermoid. Twenty-seven of the 58 patients who had symptoms apparently due to the dermoid complained of pain or a bearing-down sensation. Seventeen patients came to the clinic because of a tumor which they could feel in the lower abdomen. Attacks of acute pelvic pain were the only symptoms in 5 cases. A fistula from the vagina to the dermoid was present in 2 cases. Three tumors in this series had twisted pedicles and 2 were completely twisted off. One had implanted itself on the posterior wall of the uterus, and the other on the greater omentum; this tumor could be manipulated into the upper abdomen. In the 3 cases the torsion was chronic. Although one or two complete twists were present in all, complete loss of circulation had not resulted. In the entire series infection occurred in 3 cases. In 1 the tumors were bilateral, and both were infected. One of the other 2 was associated with a tuboövarian abscess on the same side and the other was apparently induced by a twist of the pedicle. Other types of ovarian cysts were associated with the dermoids in 17 patients. In 1 case bilateral simple cysts were present; in 4 cases simple cysts were present in the same ovary and in 8 cases simple cysts were present in the other ovary. Associated bilateral chocolate cysts were present in 1 case. A multilocular cystadenoma was in the same ovary as the dermoid in 3 cases. There was 1 case of malignant degeneration, this being a squamous-cell cancer in a woman, aged forty-eight years. Thirty-nine of the cysts in this series contained teeth, the number varying from one to twenty-eight, two or three usually being found. In most cases the teeth were buried under the skin and fibrous tissue of the *focus*, which is the name applied to the parenchymal portion of the cyst which projects into its cavity. When bone was present the teeth were usually imbedded in it, and in this series bone was present in thirty-three cysts. In only 2 cases did the bony mass superficially resemble a normal bone, a jawbone in both cases. Microscopically, squamous epithelium was found in all cases. The typical dermoid squamous epithelium resem-

bled that found in the mouth. Hair was present in all but 1 case. Typically the hair was from 10 to 15 cm. long, reddish-brown and loose, tangled or even felted. Much of it was frequently implanted at both ends, that is, growing from one end and into the opposite wall at the other. Sweat glands, closely resembling the normal sweat glands, were present in 80 cases. Tissues derived from the mesoderm were present in 94 cases, as evidenced by fat, areolar tissue, muscle, bone, cartilage and certain parts of the teeth, as the dentin. Derivatives of the entoderm were demonstrable in fifty-seven dermoids. In eight specimens an intestinal type of mucosa was found. This consisted of a single layer of columnar cells with definite crypts. In two, glands not unlike Brunner's glands were present. These gastro-intestinal structures had a thick, smooth muscle wall indefinitely arranged in two layers.

OTO-RHINO-LARYNGOLOGY

UNDER THE CHARGE OF

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The Use of Strychnine for Disturbances of Balance, in Subjective Sounds in the Ears and in Defective Hearing.—BECK (*Ztschr. f. Hals Nasen u. Ohrenh.*, 1924, **9**, 222) has experienced very beneficial results by giving strychnin in cases of subjective vertigo, tinnitus aurium and objective derangements of equilibrium. Auditory acuity was improved in 2 instances. The favorable action was thought to be due to an increased sensitiveness to stimuli from the sense organs produced by the drug. Those conditions due to vasomotor disturbances responded especially well to the strychnin therapy, so that one might expect satisfactory results in cases of cerebral vertigo associated with such vascular diseases as arteriosclerosis. The initial dose was 1 to 2 mg. daily, increasing by 1 mg. up to 6 mg. daily, and then decreasing the dose to 1 mg.

Contributions to the Study of the Sphenopalatine Ganglion.—"The sphenopalatine ganglion is the second largest nerve center in the head and the largest nerve center outside the cranial cavity. As such, it assumes a position of greatest importance to the nose and throat specialist. It innervates and is intimately connected with practically every region treated by the otorhinolaryngologist. Its distribution is so extensive as to give symptoms directly and reflexly to practically every part of the body. It involves most of the cranial nerves, the cranial and visceral autonomic system and some of the spinal nerves, with remote effects produced through parts not yet traced." Recognizing the consummate importance of this structure, RUSKIN (*Laryngoscope*, 1925, **35**, 87) describes its systemic, regional and topographic anatomical

relationships in detail, and describes a method of injecting the ganglion through the roof of the mouth by way of the posterior palatine canal. Employing a 22-gauge platinum needle, 45 mm. long, mounted on a syringe at about a 45-degree angle, with the patient in the lying position and head extended, the author locates the posterior palatine foramen by palpating the edge of the hard palate and inserting the needle 5 mm. anteriorly and about 0.75 cm. medial to the second molar tooth. The needle is then inserted through the canal to a depth of 3.5 to 4 cm. For anesthesia 1 per cent novocain with adrenalin is used. For alcoholic injection the posterior palatine canal is first located with novocain, then followed with alcohol. The following conditions have yielded to the treatment: External cricoidynia; lower jaw toothache; glossodynia; earache in case of Eustachian tube and middle-ear lesions, as well as secondary to cancer of larynx; pain of laryngeal tuberculosis and herpes of the shoulder; relief of spasm of the esophagus; relief of spasm of face and upper respiratory tract; all syphilitic headaches; malarial headache; ophthalmic migraine; dysmenorrhea; lumbago; intercostal pain (neuralgia); gastric pain; nausea and diarrhea; myalgias of neck muscles; sciatica; maxillary neuralgia; tic douleureux; sensory facial neuralgia; pain in upper teeth and sensation as though teeth were too long; feeling of foreign body in throat; persistent itching of external canal; herpes zoster oticus and taste disturbances. In addition, the author has found it valuable in producing anesthesia for tonsillectomy, radical antrum operations and for certain operations having to do with radical ethmoid, sphenoid and septal surgery. The author, concluding, considers sphenopalatine ganglion neuralgia as a combination of four syndromes: (1) Sensory facial (seventh nerve) syndrome; (2) maxillary (fifth nerve) syndrome; (3) sympathetic syndrome; (4) sphenopalatine ganglion-cell syndrome—all of which may occur singly or in combination.

Report of the Committee on the Problems of the Hard-of-Hearing, Section on Laryngology, Otology and Rhinology.—A committee, including HAYS, NEWHART, PIERCE, PHILLIPS and SHAMBAUGH (*Jour. Am. Med. Assn.*, 1924, **83**, 2094) constituted to investigate the problems of the hard of hearing, reported the following ideas on the subject, as gleaned from 150 replies to a questionnaire sent to 1000 members: "(1) The most important etiologic factors producing deafness are nose and throat conditions that directly affect the Eustachian tube. (2) Deafness is decreasing because more attention is being paid to nose and throat conditions in childhood. (3) Otosclerosis is comparatively rare; nerve deafness is rare except in syphilis and meningitis. (4) Roentgenotherapy is absolutely without value, except so far as it affects the lymphatic tissue in the nasopharynx; mechanotherapeutics or electrotherapeutics produce no beneficial results, although some forms of vibration are of temporary benefit. (5) Ethical specialists urge deaf patients to wear suitable hearing devices, to stay away from quacks and to learn lip reading."

Lung Abscess following Tonsillectomy.—"A great deal of reflection and study has been devoted to the subject of lung abscess following tonsillectomy. At the present time there are two main theories of its

origin. One is that the lung suppuration is usually due to the aspiration of adenoid or tonsil tissue, or of potentially infective blood and mucus, or the crypt content or any combination of these. The other is that a septic embolus becomes dislodged from one of the thrombosed vessels in the operative area, and finally settles in the lung where an abscess is initiated." After reciting the opinions of several surgeons, answering this questionnaire, MYERSON (*Arch. Otolaryngol.*, 1925, **1**, 137) gives the results of recent bronchoscopic studies of tonsillectomy under general anesthesia, in which 155 of 200 patients showed the presence of the tonsillectomy blood mixture in the bronchi, without a single pulmonary complication. From this the author concludes: "That the cause of these complications does not lie in the aspiration of the tonsillectomy pharyngeal content into the bronchial tree, or the factors that influence this aspiration, but rather in the failure of the evacuation of this potentially infective material and the factors that influence this failure of evacuation and expulsion from the bronchial tree and lung bed"—such factors as the cilia of the bronchial mucosa and the elasticity and compressibility of the lung tissue. Any condition, such as increased concentration and prolonged administration of ether, influenza, pneumonia or tuberculosis, which damages the pulmonary and bronchial elements, would indicate an inability to expel the aspirated material, predisposing to a site of election for a suppurative lesion. From his studies, the author admonishes that all tonsillectomy patients should be given a careful preoperative survey, with special reference to the pulmonary tract, so that "in the presence of known pulmonary disease we should be forewarned and plan our operative procedure accordingly."

The Comparative Value of Transillumination and Roentgenography in Diagnosis of Maxillary Sinus Disease (Author's Methods).—As the maxillary sinus is the most constant of all the nasal accessory sinuses, BRIGGS (*Ann. Otol., Rhinol. and Laryngol.*, 1925, **34**, 485) describes, in detail, its anatomic features. After a comprehensive review of the literature having to do with the various opinions as to the relative merits of transillumination and roentgen-ray examination of the maxillary sinus, the author describes his methods of examination. In transillumination, with the patient seated on a high stool in a very dark room, with head tilted backward, mouth open, lids closed and eyes directed downward, the 6-volt lamp, controlled by a rheostat and placed on a shank having two 45-degree angles, and so constructed as to prevent the escape of light, is placed against the lower eyelid directly below the pupil, pressed backward beyond the infraorbital ridge and directed downward toward the floor of the antrum. If not obstructed the light will illuminate the floor of the antrum and can be observed as a pink area on that part of the roof of the mouth near the molars and the buccal wall above the alveolar process. For roentgen-ray films he prefers the chin-nose position, as having the advantage of bringing the antrum nearer the plate, making a less acute angle with the central rays and, consequently, insuring less distortion. The author believes that both roentgenography and transillumination are of the greatest value in diagnosing pathologic conditions of the maxillary and frontal sinuses. The roentgen ray is superior to transillumination in outlin-

ing the anatomic relations, showing foreign bodies, as unerupted teeth, and perhaps in detailing shadows of chronic thickening of mucous membrane and bony walls. Transillumination is more reliable in acute infections and is more sensitive to the retained antral secretions. The author states that were he limited to the use of only one of these exceedingly valuable methods of examination, he would choose transillumination.

Recognition of Sinus Disease in Children.—"The work of Dean and Byfield has stimulated investigation for the relief of sinusitis in children, and has resulted in untold benefits for children suffering from 'chronic colds' due to infection of the paranasal sinuses." Although our attitude in regard to sinusitis in children is easily explained when we recall that it has never been impressed upon us that children possess sinuses prior to puberty, BARLOW (*Ann. Otol., Rhinol. and Laryngol.*, 1925, **34**, 378) emphasizes the fact that the maxillary sinus appears in the third month of fetal life and at twelve months of postfetal life is quite well developed; that the ethmoid cells are present in the latter part of the third and fourth fetal months, and that the frontal sinus may be found in the third or fourth month of fetal life, but is usually recognized only after the third or fourth year of postfetal life. He believes that an acute suppurative sinusitis in children rarely returns to normal or that the infection entirely subsides, so that a low-grade residual infection of the mucous membrane lining continues and there remains a mild type of chronic suppurative sinusitis. The most prominent manifestation of chronic sinusitis is a mucopurulent discharge from the nose—a discharge which is quite profuse, associated with a vestibulitis and frequently with excoriation of the nares. The value of roentgen ray in the diagnosis of these conditions is stressed. From the therapeutic standpoint, in the chronic forms, the author offers surgical procedures as the most effective—draining the antrum and opening the anterior ethmoids.

Direct Blood-stream Infection through the Tonsils.—Having previously shown (*Arch. Int. Med.*, 1924, **33**, 473) by photographs of microscopic sections that the epithelium lining the tonsillar crypt is more vascular than that covering the surface of the tonsil, and that the common pathologic lesion in chronic tonsillitis is a destruction of this epithelial lining, TANAKA and CROWE (*Arch. Otolaryngol.*, 1925, **1**, 510) continued the study, calling attention to the anatomic arrangement of the capillaries in the epithelium and to the large veins that lie just under the epithelium that lines the crypts in the tonsil, and to suggest that the joint lesions and other general disturbances secondary to a chronic tonsillitis may be due to bacteriemia. The bulk of the context is composed of the explanations of composite drawings of tonsils injected with India ink and photomicrographs of the tonsillar sections in selected cases. After a brief, though comprehensive, clinical résumé of focal infections of the tonsil, the authors conclude that: (1) The epithelium that lines the crypt in a normal tonsil has a rich capillary blood supply; the large collecting veins that surround each crypt lie just under the basement membrane; (2) a destruction of this epithelium, in whole or in part, is the most common microscopic finding in chronic

tonsillitis; often the lining epithelium is replaced with scar tissue and occasionally definite ulcers are found. In either instance large numbers of bloodvessels have been thrombosed and they afford a pathway for the entrance of bacteria into the blood stream.

PATHOLOGY AND BACTERIOLOGY

UNDER THE CHARGE OF

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The Etiology of Acute Appendicitis.—One hundred appendices diagnosed clinically as acute, removed by the surgical staff of the Boston City Hospital, have been studied bacteriologically and histologically by WARREN (*Am. Jour. Path.*, 1925, **1**, 2). Of these 66 were diagnosed histologically as acute, 4 as acute periappendicitis, 15 as healing appendicitis and 1 as a healed appendix with obliteration of the lumen. The method of examination was as follows: The surgeon dropped the appendix into a sterile Petri dish which was carried to the laboratory. Cultures were taken, with aseptic precautions, from the wall of the appendix and from the lumen. The appendix was then fixed *in toto* in Zenker's fluid and sections made from the same areas as those from which the cultures were taken. The bacteriologic findings in the 66 acutely inflamed appendices showed Bacillus coli to be the organism most frequently encountered, being found alone in 25 cases and combined with other organisms in 12. Streptococcus occurred alone in 6 and combined with Bacillus coli in 9. Bacillus proteus vulgaris and Bacillus pyocyaneus were each found five times. There was a scattering of other organisms. The 4 cases of acute periappendicitis all occurred in females. Of these 2 showed pneumococcus Type I, 1 Streptococcus viridans and 1 gonococcus. Of the 16 healing appendices 1 showed Bacillus coli and 1 showed Streptococcus viridans. The remainder showed no growth. All early lesions were found at the margin of the lumen, and the inflammatory reaction was similar throughout the series irrespective of the organism found. Possibly streptococcal cases were slightly more hemorrhagic. The evidence brought by the study is against the hematogenous origin of acute appendicitis.

The Origin of Adenomatous Goiter.—KLINE (*Am. Jour. Path.*, 1925, **1**, 2) reports the microscopic study of over 600 adenomatous goiters at Lakeside Hospital. At present there are two views concerning the origin of this condition, that of Beck, Woelfler, Ribbert and others who believe that it arises from multiple embryonal cell nests scattered through the tissue, which begin to enlarge from puberty onward; and

that of Virchow, Hitzig, Michaud, who contend that the nodules develop from adult thyroid tissues. As a result of the study the author inclines to the latter view. In his work he observed adult thyroid tissue apparently passing from its normal lobulation, by gradual changes, to circumscribed, encapsulated nodules histologically indistinguishable from adenomata. In sections of thyroid gland showing varying degrees of hypertrophy and hyperplasia more or less circumscribed areas are not infrequently found in which the hyperplasia is more marked than generally throughout the gland. The repeated changes in such glands to the colloid state apparently brings about in some an increase in stroma around and within the lobules causing greater circumscription of lobules than normal, or division of lobules into smaller circumscribed units. When hyperplasia occurs in these areas they gradually increase in size and become spherical in form. The capsule may be gradually acquired in one of two ways: (1) The compression of regional thyroid tissue with atrophy and replacement fibrosis thereof; (2) when the growing lobule returns to its colloid state, the older central acini usually take up more colloid than those in the periphery, which are younger. The pressure exerted toward the periphery results in atrophy and replacement fibrosis. The paper is well illustrated with plates.

Pathogenicity of Clostridium Botulinum.—An elaborate study of the conditions of toxin production of Clostridium botulinum which shows evidence of great thoroughness, skill and patience, is reported by STARIN and DACK (*Jour. Infect. Dis.*, 1925, **36**, 383). The principal strain used was one designated as M7a², a single-cell isolation, highly toxic, recovered from the Greensburg, Pa., outbreak in 1921. Casein-digest-veal-infusion broth was used as a medium and cultures were incubated three to four weeks. Elaborate aseptic precautions were used throughout the work, controls rigidly observed and all doubtful results indicated. Rabbits were injected with spores of Clostridium botulinum intravenously and intraperitoneally. Detoxified spores were fed orally to rabbits, and detoxified spores were introduced into guinea pigs intraperitoneally, intravenously, intramuscularly and orally. Detoxified spores were injected into mice in all series as controls. White rats were used in one series and were found to be markedly resistant to the action of Clostridium botulinum toxin. The influence of calcium chlorid and quinin on the pathogenicity of the spores was investigated on account of their influence on the pathogenicity of the spores of Clostridium tetani. No influence was noted that could not be attributed to the action of the calcium chlorid or quinin alone on the animal organism. There was no agreement between the findings in Clostridium botulinum and Clostridium tetani. Collodion sacs containing spores of Clostridium botulinum were introduced into the peritoneal cavities of rabbits and guinea pigs. Paraffined sacs containing sterile toxin or toxin-freed cells were also used. This part of the work presented many difficulties. Evidence was obtained of the multiplication and toxin production of the organism in the body of animals, but the exact relationship between the organisms in the sac and the host was not found. Among the constant changes found in animals dying of botulism not hitherto reported they found marked stasis of the

contents of the gall bladder, urinary bladder and stomach. Marked icterus was noted in rats. Congestion of the stomach wall was observed particularly in the stomach region, leading in some cases to definite necrosis. They conclude that detoxified spores can multiply in the animal and produce sufficient toxin to induce experimental botulism, but that the number of spores necessary to do this is quite large. The spores may remain latent in the animal body for at least as long as four months. Clostridium botulinum was recovered from widespread parts of the body after death from botulism, the highest percentage of positive results being recorded in liver, kidneys, spleen and cecum. Organs from such animals, macerated in salt solution, showed no evidence of botulism toxin. Antibody formation agglutinins in animals could be demonstrated.

Pneumonia Associated with Bacillus Abortus (Bang) in Fetuses and Newborn Calves.—A pneumonic condition in fetuses and newborn calves due to Bacillus abortus is pointed out for the first time by SMITH (*Jour. Exper. Med.*, 1925, **41**, 639). The fetuses examined are placed in three classes: Those which have not breathed, those expelled with partly inflated lungs and a number of calves killed during the first week of life which were slightly premature. A detailed description of the lungs and their pneumonic areas is given. Bacillus abortus was demonstrated in all cases. The character of the pathological process, its extent and its bearing on the epidemiology of pneumonia is indicated.

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